© THE QUEEN'S PRINTER FOR ONTARIO
2000

REPRODUCED WITH PERMISSION

L'IMPRIMEUR DE LA REINE POUR L'ONTARIO

REPRODUIT AVEC PERMISSION

micromedia
a division of IHS Canada

20 Victoria Street
Toronto, Ontario M5C 2N8
Tel.: (416) 362-5211
Toll Free: 1-800-387-2689
Fax: (416) 362-6161
Email: info@micromedia.on.ca

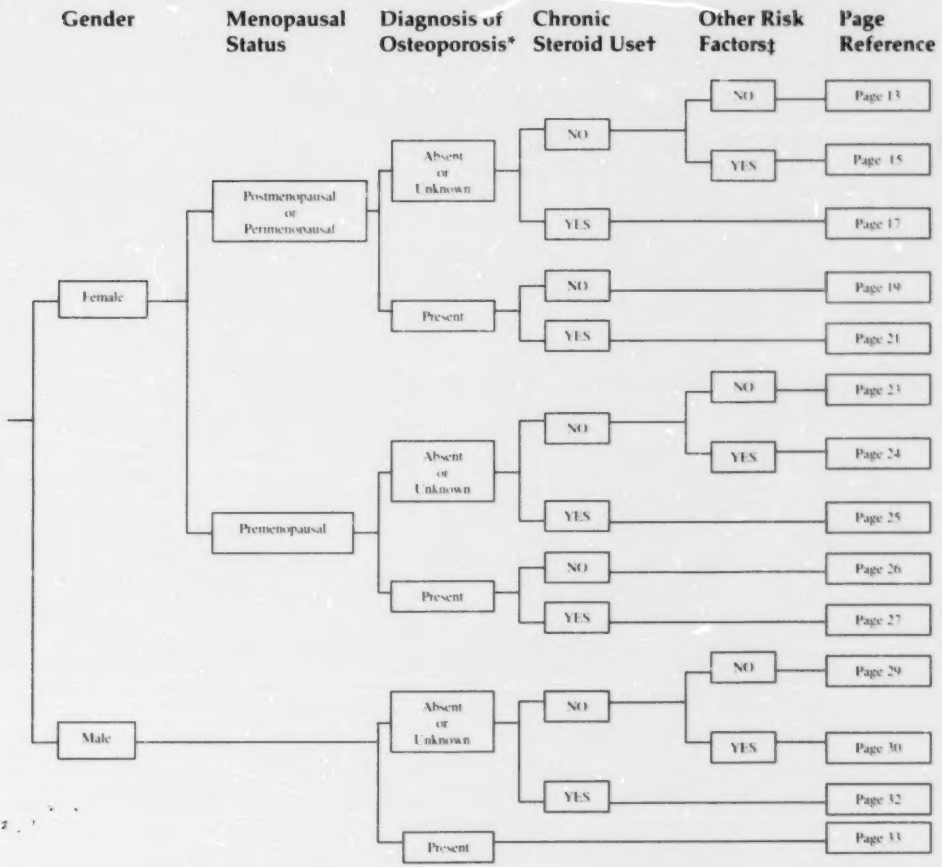
Published Fall 2000

1st Edition

Ontario Guidelines for the Prevention and Treatment of Osteoporosis

Ontario Program for Optimal Therapeutics

Guide to the Guideline



* Osteoporosis defined by:
a) a history of low trauma or fragility fracture(s), or
b) a T-score < -2.5 S.D. by DXA

† Chronic steroid use defined as a period of > 3 months with ≥ 7.5 mg/day of prednisone or equivalent continuous daily

DXA = dual x-ray absorptiometry
BMI = body mass index

‡ Presenting with one or more of the following risk factors

- current cigarette smoking
- history of hip, wrist or vertebral fractures in a first-degree relative
- early menopause
- small frame (body weight <57.8 kg or BMI < 21.2 kg/m^2), refer to page 39 for a nomogram to calculate BMI
- osteopenia (T-score between –1 and –2.5 S.D by DXA)
- advanced age (≥ 75 years)
- institutionalized
- predisposition to falls

10786

101-02445/

Ontario Guidelines for the Prevention and Treatment of Osteoporosis

Ontario Program for Optimal Therapeutics

June, 2000

For additional copies please write or call:

PUBLICATIONS ONTARIO
50 Grosvenor St.
Toronto, Ontario M7A 1N8
Telephone: (416)-326-5300 or toll-free in Ontario 1-800-668-9938.
Hearing impaired call: (416)-965-5130 or toll-free in Ontario 1-800-268-7095
Fax: (416)-326-5317

MasterCard and Visa accepted. Cheques and money orders payable to the Minister of Finance. Prepayments required.

ISBN 1-894706-05-6

Acknowledgment: Support for the development, production and distribution of this guideline was provided by the Ontario Program for Optimal Therapeutics (OPOT), made possible through a grant from the Ontario Ministry of Health and Long-Term Care.

DISCLAIMERS -- PLEASE READ CAREFULLY: This publication is designed for use by qualified health practitioners in providing health services, and is made available upon the express understanding that the authors, publisher, and other parties involved in its preparation are not providing medical or other professional advice to the general public. If required, such advice should be sought from a qualified health practitioner. This publication is not intended to replace other prescribing information, or as a substitute for the knowledge of a qualified health care provider. Nor can the guidelines take into account the unique needs of each patient or the variations in clinical resources available to a particular community or health care professional. Physicians are urged to consult drug information available in the medical literature, and from the manufacturer and other sources before prescribing.

This publication is based on information from sources believed to be reliable. While great effort has been taken to assure the completeness and accuracy of the information, it is not intended to reprint all of the information available on the subject of the publication, but rather to compile, complement and supplement other available sources. The Review Panel, publisher, printer and others contributing to the preparation of this document cannot accept liability for errors, omissions or any consequences arising from the use of the information.

Inclusion of a pharmaceutical product in these guidelines was determined solely on the basis of the Review Panel's expert professional assessment of the available evidence. It is not intended, and cannot be taken, as a recommendation that the product be included in the reimbursement policies of any drug plan or benefits manager.

Stakeholder groups were invited to participate in the development of these guidelines by reviewing and commenting upon the guidelines in draft form. These included health care professionals, professional societies, the pharmaceutical industry and the Ontario Ministry of Health and Long-Term Care.

Comments: A form is provided at the end of the document for the submission of reader's suggestions.

© 2000 Queen's Printer of Ontario

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior written permission of the publisher.

Table of Contents

Guideline Preamble 1

SECTION I: Introduction 5
- Stratification according to risk of fracture 7
- Description of Factors Increasing the Risk of Fracture 8
- Flowchart to identify the appropriate set of treatment recommendations in Section II 9

SECTION II: Treatment Recommendations 11
- Post-menopausal women without osteoporosis or risk factors 13
- Post-menopausal women without osteoporosis but with risk factors 15
- Glucocorticoid-treated post-menopausal women without osteoporosis 17
- Post-menopausal women with osteoporosis 19
- Glucocorticoid-treated post-menopausal women with osteoporosis 21
- Pre-menopausal women without osteoporosis or risk factors 23
- Pre-menopausal women without osteoporosis but with risk factors 24
- Glucocorticoid-treated pre-menopausal women without osteoporosis 25
- Pre-menopausal women with osteoporosis 26
- Glucocorticoid-treated pre-menopausal women with osteoporosis 27
- Men without osteoporosis or risk factors 29
- Men without osteoporosis but with risk factors 30
- Glucocorticoid-treated men without osteoporosis 32
- Men with osteoporosis 33

SECTION III: TREATMENT MODALITIES 35
- Drug Treatment Modalities, Available Doses and Corresponding Costs 37
- Hormone Replacement Therapy Selection and Dosing 38
- Body Mass Index Nomogram 39
- Approximate Calcium Content of Select Foods 40

REFERENCE LIST 43

COMMENT FORM 51

Preamble

Ontario Program for Optimal Therapeutics

Panel Members

Dr. Rick Adachi
Hamilton, Ontario

Dr. Tassos P. Anastassiades
Kingston, Ontario

Dr. Jacques Brown
Sainte-Fox, Quebec

Dr. Ann B. Cranney
Ottawa, Ontario

Dr. David Goltzman
Montreal, Quebec

Dr. Gillian A. Hawker
Toronto, Ontario

Dr. Anthony B. Hodsman
London, Ontario

Dr. Robert G. Josse
Toronto, Ontario

Dr. Mitchell Levine (chair)
Hamilton, Ontario

Dr. Denis O'Donnell
Hamilton, Ontario

Dr. Alex Papaioannou
Hamilton, Ontario

Dr. Nicholas Pimlott
Toronto, Ontario

Dr. Andrew Quinn
Tweed, Ontario

Dr. Rolf Sebaldt
Hamilton, Ontario

Dr. W.B. Wynveen
Simcoe, Ontario

Corresponding Stakeholders

Dr. Philip Baer
Scarborough, Ontario

Dr. George Bahsali
Moncton, New Brunswick

Dr. Susan Barr
Vancouver, British Colombia

Dr. Norm Bottum
Haliburton, Ontario

Eli Lilly Canada Inc.

Dr. Jennifer Everson
Hamilton, Ontario

Dr. Wesley Fidler
Thunder Bay, Ontario

Dr. Brian Gamble
Chatam, Ontario

Hoffman-La Roche Ltd.

ICN Canada Inc.

Dr. Shawna Johnston
Kingston, Ontario

Dr. Algis Jovaisas
Ottawa, Ontario

Dr. John Lamont
Hamilton, Ontario

Dr. Bill Leslie
Winnipeg, Manitoba

Dr. Peter McPhedran
Elora, Ontario

Merck Frosst Canada Inc.

Novartis Pharma Canada Inc.

Organon Canada Ltd

Dr. Grahame Owen
Oakville, Ontario

Pharmacia & Upjohn

Procter & Gamble
Pharmaceuticals Canada
Ltd.

Roberts Pharmaceuticals
Canada Inc.

Schering Canada Inc.

SmithKline Beecham
Pharma

Dr. John Stewart
Port Perry, Ontario

Dr. Carter Thorne
Newmarket, Ontario

Wyeth-Ayerst Canada
Inc.

Dr. Joyce Zazulak
Hamilton, Ontario

The views expressed in this document may not be representative of the views held by some of the individual participants, nor the institutions or organizations that they are affiliated with.

Guideline Preamble

Purpose of the Guidelines

These practice guidelines are designed for use by health care practitioners in the primary care setting. The intent of these guidelines is to assist the family practice physician in selecting the most appropriate drug therapy for their patients based on the best available evidence.

Guideline Development Process

The guideline development process combines critical assessment of available research evidence with expert clinical opinion of clinicians and researchers. The process is overseen by a Review Panel consisting of family physicians, relevant specialists, clinical pharmacologists, pharmacists and epidemiologists representing various regions of the province, academic and community-based clinical practice, and research. The process progresses through the following stages:

- Compilation, rigorous review and critical appraisal of evidence sources, including a thorough literature search for relevant trials, meta-analyses, practice guidelines and economic analyses.
- Preparation of a draft of the guidelines, including a grade assigned to each recommendation indicating the strength of its supporting evidence, with drugs designated "first-line" or other based on the strength of efficacy data, adverse effect profile, cost, availability, convenience and other factors.
- Review and comment by a broad spectrum of external stakeholders, including all relevant health care professionals, professional societies, pharmaceutical companies, the Ministry of Health and Long-Term Care, and consumers.
- Progressive refinement of the guidelines, and formulation in final form for publication, by the Review Panel, based on their assessment of the evidence and input from the stakeholder review.

Further details of the process used to develop this consensus guideline can be obtained by contacting OPOT at the following address:

Ontario Program for Optimal Therapeutics
708-25 Charlton Ave E
Hamilton, *ON*, L8N 1Y2

Using the guidelines

This manual is divided into 2 sections. **Section I: Introduction** contains a flow chart (Figure 1), which can be used to locate the page in Section II that has the treatment recommendation most appropriate to your patient. **Section II** contains details of the treatment recommendations including dosing information and estimated costs. The Appendices include a general overview and additional information on the evidence supporting the recommendations made in Section II.

To find the recommended treatment for your patient:

1) Refer to Figure 1 on page 9 to locate the set of treatment recommendations in Section II which best applies to your patient.
2) Turn to the appropriate page in Section II and select the therapy most suitable for your patient from the recommended treatment regimens.

Grading of Recommendations:

The evidence supporting each treatment recommendation has been evaluated by the consensus panel with respect to the appropriateness of the study design, the relevance of the study outcomes and the generalizability of the study results to the patient group in question. The following scheme has been used to grade the strength of each recommendation i.e. the strength to which the practitioner is encouraged to adhere to each recommendation based on the quality of the supportive evidence.

Grade A: **Strong recommendation**. The recommendation is based primarily upon well-designed randomized controlled trials (RCT's) or meta-analyses that assure clinically important results, such as a reduction in fracture events combined with an improvement in bone mineral density. Deviation from the recommendation is discouraged except if there are special circumstances (e.g. patient-specific contraindications, medication allergies or intolerance, previous failure on the regimen, etc.).

Grade B: **Moderate recommendation**. The recommendation is a combination of quality evidence and expert opinion. Among the possible limitations, studies may have only evaluated surrogate outcomes (e.g. improvements in bone mineral density) or have had a case-control/cohort design. Although the recommendation is based on the best available evidence, differences in interpretation may lead to some deviations from the recommendations.

Grade C: **Weak recommendation**. The recommendation is based principally upon expert opinion. Deviations from the recommendation may be appropriate where circumstances or experience conflict with the recommendations.

Cost of Treatments:

In Section II the cost of each treatment is reported as an average monthly cost. For prescription items, this cost was calculated using the 'best available price' listed in the Ontario Drug Benefit Formulary or supplied by the manufacturer. For over-the-counter items, a number of pharmacies in the greater Toronto area were contacted and an average cost was calculated. A pharmacist's professional fee was not included in the cost of prescription items (Typical fees range from $2 to $12).

Section I

Introduction

Ontario Program for Optimal Therapeutics

Introduction

Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fractures[1,2]. The World Health Organization has defined osteoporosis in terms of bone mineral density (BMD). Individuals with a T-score below -2.5 SD are defined as having osteoporosis[3]. The impact of this disease is considerable. Approximately 40% of Caucasian women aged 50, will suffer from a hip fracture, vertebral fracture and/or wrist fracture in their lifetime[4]. In 1996, in Ontario alone there were 9,382 patients hospitalized for hip fractures, 26% of whom were men[5]. In 1993, the cost of illness due to osteoporosis and its complications in Canada was estimated at 1.3 billion dollars[6].

The spectrum of management of osteoporosis ranges from early prevention (treatment of patients at risk of losing bone mass) to late prevention (treatment of patients who have already lost significant bone mass) to treatment of patients who have already fractured and are at high risk of suffering further fractures[7,8].

In order to facilitate the management of this condition, a number of practice guidelines and consensus statements have been published[7,9,10]. Over the past few years important new information in the area of treatment has been published. For example, until recently there has been only limited data supporting the use of bisphosphonate therapy in postmenopausal women. Consequently, hormone replacement therapy has been regarded as the treatment of choice. Although the following guidelines correspond in many ways to previous guidelines, the guidelines also reflect the 'new evidence' that has emerged over the past few years.

These guidelines are intended to assist the general practitioner select the pharmacologic regimen most appropriate for their patients. A thorough discussion of the treatment options with the patient should always accompany the final selection of a treatment regimen since patient preference, suitability to patient lifestyle and treatment goals will likely influence medication adherence and, as a consequence, the success of the regimen.

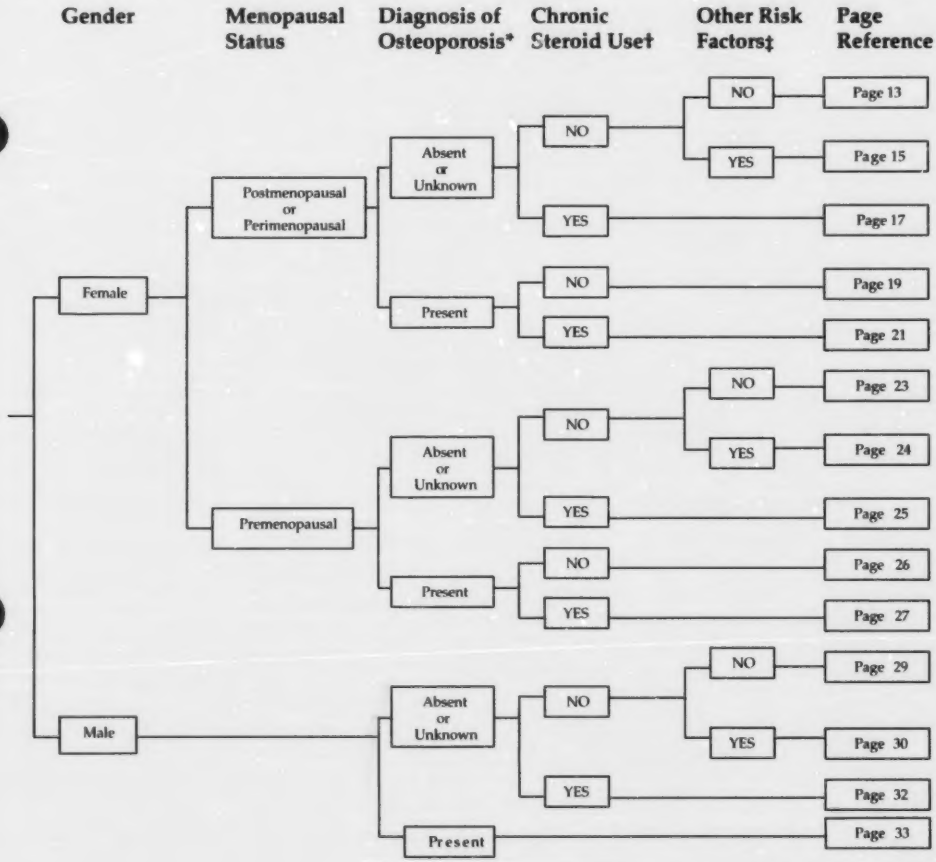
Stratification according to risk of fracture

The decision to initiate osteoporosis therapy is based, at least in part, on an assessment of an individual's future risk of osteoporosis-related morbidity and mortality. These practice guidelines have been divided into patient groups that reflect the individual's risk of osteoporotic fractures and the inclusion criteria used in the clinical trials.

Table 1 - Description of Factors Increasing the Risk of Fracture

RISK FACTOR	DESCRIPTION
Bone Mineral Density	Bone mineral density (BMD) has been widely reported as an objective predictor of osteoporotic fracture(s)[11-13]. The identification of low bone mass is associated with an overall increase risk of fractures regardless of the site that is measured[14]. BMD results are usually reported in terms of the number of standard deviations (SD) above or below the mean peak bone mass of healthy 25-35 year-old females. BMD reported in these units is referred to as a T-score[15]. The World Health Organization has defined osteoporosis in non-fractured individuals in terms of BMD. Individuals with a T-score below -2.5 SD are defined as having osteoporosis[3]. Osteopenia has been defined as a T-score between -1 SD and -2.5 SD at any site[3]. One US study reported that 84% of women aged 80+ have BMD more than 2 SD below the mean for young normal women. It is estimated that 25% of caucasian women in the US aged 30+ have BMD more than 2 SD below the mean for young normal women in 1990[4].
Existing Osteoporotic Fractures	A history of fractures has been identified as an independent risk factor for osteoporosis[13]. Fractures suggestive of osteoporosis include non-traumatic vertebral fractures and non-vertebral fractures (e.g. fractures of the hip or wrist) resulting from normal everyday activities (e.g. falling from standing height). The presence of fragility fractures of the wrist, hip and/or vertebra or the detection of low bone mineral density (T-score < -2.5 SD) confirms a diagnosis of osteoporosis. These guidelines have grouped these 2 factors together since the implications for treatment are identical.
Ovarian Hormone Status in Women	Ovarian hormone status has a dramatic impact on the rate of bone loss in women[16]. Post-menopausal and post-oophorectomized women have estrogen deficiency which requires similar treatment measures. Hormone status and gender are important considerations and have been incorporated into the treatment stratification.
Glucocorticoid use	The pathology and treatment of glucocorticoid-induced osteoporosis are distinct from osteoporosis secondary to estrogen deficiency or age-related causes. The high prevalence of this variation of osteoporosis can be largely attributed to chronic conditions such as severe asthma and arthritis where glucocorticoids may be important components of therapy.
Current Cigarette Smoking	Current cigarette smokers appear to have accelerated bone loss, lower bone mass and a higher incidence of hip fractures as compared to nonsmokers and past smokers[17].
Low Body Weight <57.8 Kg or Body Mass Index <21.2 kg/m^2	Low body weight or body mass index may be associated with a smaller skeletal frame and a higher risk of fracture with progressive bone loss[18-21]. A body weight < 57.8 kg corresponds to the lowest quartile of women > 65 years in the SOF study[22] and a body mass index < 21.2 kg/m^2 corresponds to the lowest quintile of women ≥ 50 years in the MEDOS study[23]. Refer to page 29 for a nomogram to calculate BMI.
History Of Fracture In First-Degree Relative	A family history of osteoporotic fractures has been identified as an independent risk factor.
Early Menopause	Women experiencing menopause before the age of 45 years are at risk of early reductions in estrogen concentrations resulting in premature loss of calcium bone stores and reduced bone density.
Hypogonadism in Men or in Premenopausal Women	A prolonged period of hypogonadism (>1 year) which is often characterized by late menarche or pre-menopausal amenorrhea in women and low testosterone concentrations in men can lead to reduced bone density secondary to changes in hormone-mediated bone remodelling.
Other Risk Factors[23]	• poor calcium intake (lifelong) • alcoholism • recurrent falls • low level of weight-bearing activity • caucasian race • advanced age (≥ 75 years) • dementia • poor health/frailty • impaired eyesight despite adequate correction • institutionalized

Figure 1 – Flowchart to identify the appropriate set of treatment recommendations in Section II



* Osteoporosis defined by:
a) a history of low trauma or fragility fracture(s), or
b) a T-score < -2.5 S.D. by DXA

† Chronic steroid use defined as a period of > 3 months with ≥ 7.5 mg/day of prednisone or equivalent continuous daily

DXA = dual x-ray absorptiometry
BMI = body mass index

‡ Presenting with one or more of the following risk factors:

- current cigarette smoking
- history of hip, wrist or vertebral fractures in a first-degree relative
- early menopause
- small frame (body weight <57.8 kg or BMI < 21.2 kg/m^2), refer to page 39 for a nomogram to calculate BMI
- osteopenia (T-score between –1 and –2.5 S.D by DXA)
- advanced age (≥ 75 years)
- institutionalized
- predisposition to falls

Section II

Treatment Recommendations

Ontario Program for Optimal Therapeutics

M121

IMPORTANT NOTE CONCERNING THE FOLLOWING PAGES

THE PAGES WHICH FOLLOW HAVE BEEN FILMED TWICE IN ORDER TO OBTAIN THE BEST REPRODUCTIVE QUALITY

USERS SHOULD CONSULT ALL THE PAGES REPRODUCED ON THE FICHE IN ORDER TO OBTAIN A COMPLETE READING OF THE TEXT.

REMARQUE IMPORTANTE CONCERNANT LES PAGES QUI SUIVENT

LES PAGES SUIVANTES ONT ÉTÉ REPRODUITES EN DOUBLE AFIN D'AMÉLIORER LA QUALITÉ DE REPRODUCTION

LES UTILISATEURS DOIVENT CONSULTER TOUTES LES PAGES REPRODUITES SUR LA FICHE AFIN D'OBTENIR LA LECTURE DU TEXTE INTÉGRAL

micromedia
a division of IHS Canada

20 Victoria Street
Toronto, Ontario M5C 2N8
Tel.: (416) 362-5211
Toll Free: 1-800-387-2689
Fax: (416) 362-6161
Email: info@micromedia.on.ca

Post-menopausal women without osteoporosis or risk factors

Description: Post-menopausal (or oophorectomized)
AND No previous osteoporotic fractures
AND No other risk factors:

- no osteopenia (defined as having a T-score between -2.5 SD and –1.0 SD)
- no current cigarette smoking
- no history of hip, wrist or vertebral fractures in a first-degree relative
- no early menopause (before 45 years of age)
- no small frame (body weight <57.8 kg or BMI <21.2 kg/m^2)
- not advanced in age (≥ 75 years)
- not institutionalized
- not predisposed to falls

Primary Prevention Therapy:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Estrogen†**	conjugated estrogens 0.625 mg daily or alternative[15]	B	$2.35
	OR			
	Bisphosphonate	alendronate 5-10 mg daily	B	$41.48 to $52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)‖	B	$12.23
	OR			
	Selective estrogen receptor modulator‡	raloxifene 60 mg daily	B	$43.68
If using estrogen and uterus is intact ADD	**Progesterone**	medroxyprogesterone acetate 2.5 mg daily§		$2.49

Post-menopausal women without osteoporosis or risk factors

Description: Post-menopausal (or oophorectomized)
AND No previous osteoporotic fractures
AND No other risk factors:

- no osteopenia (defined as having a T-score between -2.5 SD and –1.0 SD)
- no current cigarette smoking
- no history of hip, wrist or vertebral fractures in a first-degree relative
- no early menopause (before 45 years of age)
- no small frame (body weight <57.8 kg or BMI <21.2 kg/m^2)
- not advanced in age (≥ 75 years)
- not institutionalized
- not predisposed to falls

Primary Prevention Therapy:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Estrogen**[7]	conjugated estrogens 0.625 mg daily or alternative[18]	B	$2.35
	OR			
	Bisphosphonate	alendronate 5-10 mg daily	B	$41.48 to $52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)[8]	B	$12.23
	OR			
	Selective estrogen receptor modulator[9]	raloxifene 60 mg daily	B	$43.68
If using estrogen and uterus is intact ADD	**Progesterone**	medroxyprogesterone acetate 2.5 mg daily[5]		$2.49

NOTES:

BMI = body mass index (Refer to page 39 for a nomogram to calculate BMI)

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods.

† Contraindications to estrogen therapy:

Absolute contraindications:

- a history of unexplained vaginal bleeding
- active liver disease
- breast cancer
- active vascular thrombosis

Relative contraindications:

- migraine headaches
- a history of thromboembolism
- familial hypertriglyceridemia
- uterine leiomyomas (fibroids)
- endometriosis
- gall bladder or chronic liver disease
- uterine cancer
- a family history of breast cancer[16,17,21]

‡ There is growing evidence that lower doses of conjugated estrogens (i.e. 0.3 mg daily) when combined with appropriate calcium supplementation may be adequate. Lower doses should be considered in women unable to tolerate 0.625 mg daily.

§ Refer to page 37 for a complete list of estrogen and progestogen alternatives.

|| To ease administration of this cyclical regimen, the manufacturer packages etidronate and calcium sequentially in a blister pack format called Didrocal®. Administer 1 Didrocal tablet daily.

¶ Contraindications to raloxifene include a history of thromboembolic events (e.g. deep venous thrombosis, pulmonary embolism and retinal vein thrombosis).
Unlike estrogen therapy, women with an intact uterus do not require progestogen supplements.

References supporting these recommendations: 16,25-45

Post-menopausal women without osteoporosis but with risk factors

Description: Post-menopausal (or oophorectomized)
AND No previous osteoporotic fracture(s)
AND One or more of the following risk factors:

- T-score between -2.5 SD and -1 SD
- current cigarette smoking
- history of hip, wrist or vertebral fractures in a first-degree relative
- early menopause
- small frame (body weight <57.8 kg or BMI <21.2 kg/m^2)
- advanced age (≥ 75 years)
- institutionalized
- predisposition to falls

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	**calcium 1000 mg daily**	**B[†]**	**$2.19**
AND	**Vitamin D supplement**	**vitamin D 800 IU daily**	**B[†]**	**$2.02**
AND	**Estrogens[‡]**	**conjugated estrogens 0.625 mg daily or alternative[§‖]**	**B**	**$2.35**
If using estrogen and uterus is intact **ADD**	**Progesterone**	**medroxyprogesterone acetate 2.5 mg daily[‖]**		**$2.49**

Special Circumstances:

If unable or unwilling to use estrogen therapy **USE**	**Bisphosphonate[¶]**	**alendronate 5-10 mg daily**	**B**	**$41.48 to $52.65**
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)**	**B**	**$12.23**
		OR		
		risedronate 5 mg daily	**B[††]**	**$50.49**
	OR			
	Selective estrogen receptor modulator[‡‡]	**raloxifene 60 mg daily**	**B**	**$43.68**

Post-menopausal women without osteoporosis but with risk factors

Description: Post-menopausal (or oophorectomized)
AND No previous osteoporotic fracture(s)
AND One or more of the following risk factors:

- T-score between -2.5 SD and -1 SD
- current cigarette smoking
- history of hip, wrist or vertebral fractures in a first-degree relative
- early menopause
- small frame (body weight <57.8 kg or BMI <21.2 kg/m^2)
- advanced age (≥ 75 years)
- institutionalized
- predisposition to falls

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B[†]	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B[†]	$2.02
AND	**Estrogens**[‡]	conjugated estrogens 0.625 mg daily or alternative[‡,||]	B	$2.35
If using estrogen and uterus is intact ADD	**Progesterone**	medroxyprogesterone acetate 2.5 mg daily[||]		$2.49

Special Circumstances:

If unable or unwilling to use estrogen therapy USE	**Bisphosphonate**[¶]	alendronate 5-10 mg daily	B	$41.48 to $52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)**	B	$12.23
		OR		
		risedronate 5 mg daily	B[††]	$50.49
	OR			
	Selective estrogen receptor modulator[‡‡]	raloxifene 60 mg daily	B	$43.68

NOTES:

BMI = body mass index (Refer to page 39 for a nomogram to calculate BMI)

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods. If combined with etidronate therapy, calcium supplements need not be taken during the 14 days of each cycle when etidronate is given.

† This is a grade A recommendation in the institutionalized elderly.

‡ Contraindications to estrogen therapy:

Absolute contraindications:

- a history of unexplained vaginal bleeding
- active liver disease
- breast cancer
- active vascular thrombosis

Relative contraindications:

- migraine headaches
- a history of thromboembolism
- familial hypertriglyceridemia
- uterine leiomyomas (fibroids)
- endometriosis
- gall bladder or chronic liver disease
- uterine cancer
- a family history of breast cancer[16,17,24]

§ There is growing evidence that lower doses of conjugated estrogens (i.e. 0.3 mg daily) when combined with appropriate calcium supplementation may be adequate. Lower doses should be considered in women unable to tolerate 0.625 mg daily.

|| Refer to page 37 for a complete list of estrogen and progestogen alternatives.

¶ Do not stop hormone replacement therapy (HRT) if the patient is presently receiving it. The combined use of HRT and bisphosphonate therapy is safe and may provide additive effects on BMD[46-48].

** To ease administration of this cyclical regimen, the manufacturer packages etidronate and calcium sequentially in a blister pack format called Didrocal®. Administer 1 Didrocal tablet daily.

†† Current evidence is available primarily in abstract form. Full publications of clinical trials in peer-reviewed journals are imminent.

‡‡ Contraindications to raloxifene include a history of thromboembolic events (e.g. deep venous thrombosis, pulmonary embolism and retinal vein thrombosis).
Unlike estrogen therapy, women with an intact uterus do not require progestogen supplements.

References supporting these recommendations: 35-45

Glucocorticoid-treated post-menopausal women without osteoporosis

Description: Post-menopausal (or oophorectomized)
AND No previous osteoporotic fracture
AND Starting/receiving long term glucocorticoid therapy (≥ 3 months with ≥ 7.5 mg/day of prednisone or equivalent)

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Bisphosphonate†**	alendronate 5-10 mg daily‡	A	$41.48 to $52.65
		OR		$12.23
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)§	B	
		OR		
		risedronate 5 mg daily	A	$50.49

Special Circumstances:

If unable or unwilling to use a bisphosphonate USE	**Estrogen‖**	conjugated estrogens 0.625 mg daily or alternative¶	C	$2.35
If using estrogen and uterus is intact ADD	**Progestogens**	medroxyprogesterone acetate 2.5 mg daily¶		$2.49
If unable or unwilling to use bisphosphonate or estrogen USE	**Calcitonin**	calcitonin 100 IU subcutaneously daily	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily	B	$49.00

Glucocorticoid-treated post-menopausal women without osteoporosis

Description: Post-menopausal (or oophorectomized)
AND No previous osteoporotic fracture
AND Starting/receiving long term glucocorticoid therapy (≥ 3 months with ≥ 7.5 mg/day of prednisone or equivalent)

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement[4]	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Bisphosphonate**[5]	alendronate 5-10 mg daily[1]	A	$41.48 to $52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)[6]	B	$12.23
		OR		
		risedronate 5 mg daily	A	$50.49

Special Circumstances:

If unable or unwilling to use a bisphosphonate USE	**Estrogen**	conjugated estrogens 0.625 mg daily or alternative[3]	C	$2.35
If using estrogen and uterus is intact ADD	**Progestogens**	medroxyprogesterone acetate 2.5 mg daily[3]		$2.49
If unable or unwilling to use bisphosphonate or estrogen USE	**Calcitonin**	calcitonin 100 IU subcutaneously daily	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily	B	$49.00

NOTES:

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods. If combined with etidronate therapy, calcium supplements need not be taken during the 14 days of each cycle when etidronate is given.

† Do not stop hormone replacement therapy (HRT) if the patient is presently receiving it. The combined use of HRT and bisphosphonate therapy is safe and may provide additive effects on BMD[46-48].

‡ Patients should be started at alendronate 10 mg daily for the first year.

§ To ease administration of this cyclical regimen, the manufacturer packages etidronate and calcium sequentially in a blister pack format called Didrocal®. Administer 1 Didrocal tablet daily.

|| Contraindications to estrogen therapy:

Absolute contraindications:

- a history of unexplained vaginal bleeding
- active liver disease
- breast cancer
- active vascular thrombosis

Relative contraindications

- migraine headaches
- a history of thromboembolism
- familial hypertriglyceridemia
- uterine leiomyomas (fibroids)
- endometriosis
- gall bladder or chronic liver disease
- uterine cancer
- a family history of breast cancer[16,17,24]

¶ Refer to page 37 for a complete list of estrogen and progestogen alternatives.

References supporting these recommendations: 48-82

Post-menopausal women with osteoporosis

Description: Post-menopausal (or oophorectomized)
AND Previous osteoporotic fracture **or** T-score < -2.5 SD

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	**calcium 1000 mg daily**	**B[1]**	**$2.19**
AND	**Vitamin D supplement**	**vitamin D 800 IU daily**	**B[1]**	**$2.02**
AND	**Estrogen[†]**	**conjugated estrogens 0.625 mg daily or alternative[‡‖]**	**B**	**$2.35**
	OR/AND[¶]			
	Bisphosphonate**	**alendronate 10 mg daily**	**A**	**$52.65**
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle) [††]	**B**	**$12.23**
		OR		
		risedronate 5 mg daily	**A**	**$50.49**
	OR/AND[¶]			
	Selective estrogen receptor modulator[§§]	**raloxifene 60 mg daily**	**A[‖‖]**	**$43.68**
***If using estrogen and uterus is intact* ADD**	**Progestogens**	**medroxyprogesterone acetate 2.5 mg daily[‖]**		**$2.49**

Special Circumstances:

If unable or unwilling to use estrogen therapy, bisphosphonate therapy and raloxifene ADD	**Calcitonin**	**calcitonin 100 IU subcutaneously daily**	**B**	**$261.64**
		OR		
		calcitonin 200 IU intranasally daily	**B**	**$49.00**
***If immobilized and with acute fracture(s) and not already receiving calcitonin* ADD**	**Calcitonin**	**calcitonin 100 IU subcutaneously daily for 6-12 weeks**	**B**	**$261.64**
		OR		
		calcitonin 200 IU intranasally daily for 6-12 weeks	**B**	**$49.00**

Post-menopausal women with osteoporosis

Description: Post-menopausal (or oophorectomized)
AND Previous osteoporotic fracture **or** T-score < -2.5 SD

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOMMENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B[‡]	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B[‡]	$2.02
AND	**Estrogen**[†]	conjugated estrogens 0.625 mg daily or alternative[¶‖]	B	$2.35
	OR/AND[†]			
	Bisphosphonate**	alendronate 10 mg daily	A	$52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle) **	B	$12.23
		OR		
		risedronate 5 mg daily	A	$50.49
	OR/AND[†]			
	Selective estrogen receptor modulator**	raloxifene 60 mg daily	A[‡‡]	$43.68
If using estrogen and uterus is intact ADD	**Progestogens**	medroxyprogesterone acetate 2.5 mg daily[¶]		$2.49

Special Circumstances:

If unable or unwilling to use estrogen therapy, bisphosphonate therapy and raloxifene ADD	**Calcitonin**	calcitonin 100 IU subcutaneously daily	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily	B	$49.00
If immobilized and with acute fracture(s) and not already receiving calcitonin ADD	**Calcitonin**	calcitonin 100 IU subcutaneously daily for 6-12 weeks	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily for 6-12 weeks	B	$49.00

NOTES:

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods. If combined with etidronate therapy, calcium supplements need not be taken during the 14 days of each cycle when etidronate is given.

† This is a grade A recommendation in the institutionalized elderly.

‡ Contraindications to estrogen therapy:

Absolute contraindications

- a history of unexplained vaginal bleeding
- active liver disease
- breast cancer
- active vascular thrombosis

Relative contraindications

- migraine headaches
- a history of thromboembolism
- familial hypertriglyceridemia
- uterine leiomyomas (fibroids)
- endometriosis
- gall bladder or chronic liver disease
- uterine cancer
- a family history of breast cancer[16,17,24]

§ There is growing evidence that lower doses of conjugated estrogens (i.e. 0.3 mg daily) when combined with appropriate calcium supplementation may be adequate. Lower doses should be considered in women unable to tolerate 0.625 mg daily.

|| Refer to page 37 for a complete list of estrogen and progestogen alternatives.

¶ If the patient exhibits multiple risk factors the combination of a bisphosphonate with either an estrogen or a selective estrogen receptor modulator may be used.

** Do not stop hormone replacement therapy (HRT) if the patient is presently receiving it. The combined use of HRT and bisphosphonate therapy is safe and may provide additive effects on BMD (extrapolated from non-glucocorticoid users)[46-48].

†† To ease administration of this cyclical regimen, the manufacturer packages etidronate and calcium sequentially in a blister pack format called Didrocal®. Administer 1 Didrocal tablet daily.

‡‡ Current evidence is limited to vertebral fracture data.

§§ Contraindications to raloxifene include a history of thromboembolic events (e.g. deep venous thrombosis, pulmonary embolism and retinal vein thrombosis).
Unlike estrogen therapy, women with an intact uterus do not require progestogen supplements.

References supporting these recommendations: 35,36,38,48,51,83-111

Glucocorticoid-treated post-menopausal women with osteoporosis

Description: Post-menopausal (or oophorectomized)
AND Previous osteoporotic fracture **or** T-score < -2.5 SD
AND Starting/receiving long term glucocorticoid therapy (≥ 3 months with ≥ 7.5 mg/day of prednisone or equivalent)

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Bisphosphonate†**	alendronate 10 mg daily	A	$52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)‡	B	$12.23
		OR		
		risedronate 5 mg daily	A	$50.49

Special Circumstances:

If unable or unwilling to use a bisphosphonate USE	**Estrogen§**	conjugated estrogens 0.625 mg daily or alternative‖	C	$2.35
If using estrogen and uterus is intact ADD	**Progestogens**	medroxyprogesterone acetate 2.5 mg daily‖		$2.49
If unable or unwilling to use bisphosphonate or estrogen USE	**Calcitonin**	calcitonin 100 IU subcutaneously daily	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily	B	$49.00
If immobilized and with acute fracture(s) and not already receiving calcitonin ADD	**Calcitonin**	calcitonin 100 IU subcutaneously for 6-12 weeks	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily for 6-12 weeks	B	$49.00

Glucocorticoid-treated post-menopausal women with osteoporosis

Description: Post-menopausal (or oophorectomized)
AND Previous osteoporotic fracture **or** T-score < -2.5 SD
AND Starting/receiving long term glucocorticoid therapy (≥ 3 months with ≥ 7.5 mg/day of prednisone or equivalent)

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement[e]	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Bisphosphonate**[f]	alendronate 10 mg daily	A	$52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)[i]	B	$12.23
		OR		
		risedronate 5 mg daily	A	$50.49

Special Circumstances:

If unable or unwilling to use a bisphosphonate USE	**Estrogen**[g]	conjugated estrogens 0.625 mg daily or alternative[ii]	C	$2.35
If using estrogen and uterus is intact ADD	**Progestogens**	medroxyprogesterone acetate 2.5 mg daily[ii]		$2.49
If unable or unwilling to use bisphosphonate or estrogen USE	**Calcitonin**	calcitonin 100 IU subcutaneously daily	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily	B	$49.00
If immobilized and with acute fracture(s) and not already receiving calcitonin ADD	**Calcitonin**	calcitonin 100 IU subcutaneously for 6-12 weeks	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily for 6-12 weeks	B	$49.00

NOTES:

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods. If combined with etidronate therapy, calcium supplements need not be taken during the 14 days of each cycle when etidronate is given.

† Do not stop hormone replacement therapy (HRT) if the patient is presently receiving it. The combined use of HRT and bisphosphonate therapy is safe and may provide additive effects on BMD (extrapolated from non-glucocorticoid users)[69–81].

‡ To ease administration of this cyclical regimen, the manufacturer packages etidronate and calcium sequentially in a blister pack format called Didrocal®. Administer 1 Didrocal tablet daily.

§ Contraindications to estrogen therapy:

Absolute contraindications

- a history of unexplained vaginal bleeding
- active liver disease
- breast cancer
- active vascular thrombosis

Relative contraindications

- migraine headaches
- a history of thromboembolism
- familial hypertriglyceridemia
- uterine leiomyomas (fibroids)
- endometriosis
- gall bladder or chronic liver disease
- uterine cancer
- a family history of breast cancer[16,17,21]

|| Refer to page 37 for complete a list of estrogen and progestogen alternatives.

References supporting these recommendations: 48,49,52-80

Pre-menopausal women without osteoporosis or risk factors

Description: Pre-menopausal (age ≥ 19 years)
AND No previous osteoporotic fracture
AND No other risk factors:

- normal BMD (T-score > -2.5 S.D.) or unknown
- not currently smoking
- no history of hip, wrist or vertebral fractures in a first-degree relative
- body weight ≥ 57.8 kg or BMI ≥ 21.2 kg/m^2
- no prolonged period of amenorrhea (> 1 year) or late menarche
- not institutionalized
- not predisposed to falls

Primary Prevention Therapy:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	**calcium 1000 mg daily**	C	**$2.19**
AND	**Vitamin D supplement**	**vitamin D 800 IU daily**	C	**$2.02**

NOTES:

BMI = body mass index (Refer to page 39 for a nomogram to calculate BMI)

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods.

No references are available

Pre-menopausal women without osteoporosis or risk factors

Description: Pre-menopausal (age ≥ 19 years)
AND No previous osteoporotic fracture
AND No other risk factors:

- normal BMD (T-score > -2.5 S.D.) or unknown
- not currently smoking
- no history of hip, wrist or vertebral fractures in a first-degree relative
- body weight ≥ 57.8 kg or BMI ≥ 21.2 kg/m²
- no prolonged period of amenorrhea (> 1 year) or late menarche
- not institutionalized
- not predisposed to falls

Primary Prevention Therapy:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	C	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	C	$2.02

NOTES:

BMI = body mass index (Refer to page 39 for a nomogram to calculate BMI)

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods.

No references are available

Pre-menopausal women without osteoporosis but with risk factors

Description: Pre-menopausal (age > 19 years)
AND No previous osteoporotic fracture(s)
AND One or more of the following risk factors:

- T-score between -2.5 SD and -1 SD
- current cigarette smoking
- history of hip, wrist or vertebral fractures in a first-degree relative
- small frame (body weight <57.8 kg or BMI <21.2 kg/m)
- institutionalized
- predisposition to falls

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02

Special Circumstances:

If amenorrheic not due to anorexia ADD	**Oral contraceptives**	Any available brand of combination oral contraceptive	C	$13.04

NOTES:

BMI = body mass index (Refer to page 39 for a nomogram to calculate BMI)

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods.

References supporting these recommendations: 112-114

Glucocorticoid-treated post-menopausal women without osteoporosis

Description: Pre-menopausal (age ≥ 19 years)
AND No previous osteoporotic fracture
AND Starting/receiving long term glucocorticoid therapy (≥ 3 months with ≥ 7.5 mg/day of prednisone or equivalent)

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Bisphosphonate†**	alendronate 5-10 mg daily‡	B	$41.48 to $52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)§	B	$12.23
		OR		
		risedronate 5 mg daily	B	$50.49

Special Circumstances:

If amenorrheic not due to anorexia ADD	**Oral contraceptives**	Any available brand of combination oral contraceptive	C	$13.04

NOTES:

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods. If combined with etidronate therapy, calcium supplements need not be taken during the 14 days of each cycle when etidronate is given.

† Bisphosphonate therapy is absolutely contraindicated in pregnancy due its potential teratogenic effects. Contraception should be strongly encouraged in sexually active women. The risks and benefits of longterm bisphosphonate therapy in this patient population are unknown.

‡ Patients should be started at alendronate 10 mg for the first year.

§ To ease administration of this cyclical regimen, the manufacturer packages etidronate and calcium sequentially in a blister pack format called Didrocal®. Administer 1 Didrocal tablet daily.

References supporting these recommendations: 49,52,54,112

Pre-menopausal women without osteoporosis but with risk factors

Description: Pre-menopausal (age > 19 years)
AND No previous osteoporotic fracture(s)
AND One or more of the following risk factors:

- T-score between -2.5 SD and -1 SD
- current cigarette smoking
- history of hip, wrist or vertebral fractures in a first-degree relative
- small frame (body weight <57.8 kg or BMI <21.2 kg/m^2)
- institutionalized
- predisposition to falls

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	**calcium 1000 mg daily**	**B**	**$2.19**
AND	**Vitamin D supplement**	**vitamin D 800 IU daily**	**B**	**$2.02**

Special Circumstances:

If amenorrheic not due to anorexia **ADD**	**Oral contraceptives**	**Any available brand of combination oral contraceptive**	**C**	**$13.04**

NOTES:

BMI = body mass index (Refer to page 39 for a nomogram to calculate BMI)

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods.

References supporting these recommendations: 112-114

Glucocorticoid-treated post-menopausal women without osteoporosis

Description: Pre-menopausal (age ≥ 19 years)
AND No previous osteoporotic fracture
AND Starting/receiving long term glucocorticoid therapy (≥ 3 months with ≥ 7.5 mg/day of prednisone or equivalent)

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Bisphosphonate†**	alendronate 5-10 mg daily‡ OR	B	$41.48 to $52.65
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)§ OR	B	$12.23
		risedronate 5 mg daily	B	$50.49

Special Circumstances:

If amenorrheic not due to anorexia ADD	**Oral contraceptives**	Any available brand of combination oral contraceptive	C	$13.04

NOTES:

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods. If combined with etidronate therapy, calcium supplements need not be taken during the 14 days of each cycle when etidronate is given.

† Bisphosphonate therapy is absolutely contraindicated in pregnancy due its potential teratogenic effects. Contraception should be strongly encouraged in sexually active women. The risks and benefits of longterm bisphosphonate therapy in this patient population are unknown.

‡ Patients should be started at alendronate 10 mg for the first year.

§ To ease administration of this cyclical regimen, the manufacturer packages etidronate and calcium sequentially in a blister pack format called Didrocal®. Administer 1 Didrocal tablet daily.

References supporting these recommendations: 49,52,54,112

Pre-menopausal women with osteoporosis

Description: Pre-menopausal (age ≥ 19 years) and not oophorectomized
AND previous osteoporotic fracture **or** T-score < -2.5 SD

PATIENTS MEETING THIS CRITERIA REQUIRE REFERRAL TO A SPECIALIST FOR INVESTIGATION OF ETIOLOGY.

No references available

Glucocorticoid-treated pre-menopausal women with osteoporosis

Description: Pre-menopausal (age ≥ 19 years)
AND a history of osteoporotic fracture(s) **or** T-score < -2.5 SD
AND receiving long term glucocorticoid therapy (≥ 3 months with ≥ 7.5 mg/day of prednisone or equivalent)*

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement[†]	calcium 1000 mg daily	B[‡]	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B[‡]	$2.02
AND	**Bisphosphonate**[§]	alendronate 10 mg daily	B[‡]	$52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)[‖]	B[‡]	$12.23
		OR		
		risedronate 5 mg daily	B[‡]	$50.49

Special Circumstances:

If amenorrheic not due to anorexia ADD	**Oral contraceptives**	Any available brand of combination oral contraceptive	C[¶]	$13.04
If unable or unwilling to use bisphosphonate USE	**Calcitonin**	calcitonin 100 IU subcutaneously daily	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily	B	$49.00
If immobilized and with acute fracture(s) and not already receiving calcitonin ADD	**Calcitonin**	calcitonin 100 IU subcutaneously for 6-12 weeks	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily for 6-12 weeks	B	$49.00

Glucocorticoid-treated pre-menopausal women with osteoporosis

Description: Pre-menopausal (age ≥ 19 years)
AND a history of osteoporotic fracture(s) **or** T-score < -2.5 SD
AND receiving long term glucocorticoid therapy (≥ 3 months with ≥ 7.5 mg/day of prednisone or equivalent)*

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOMMENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement[†]	calcium 1000 mg daily	B[‡]	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Bisphosphonate**[§]	alendronate 10 mg daily	B	$52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)[‖]	B[‡]	$12.23
		OR		
		risedronate 5 mg daily	B[‡]	$50.49

Special Circumstances:

If amenorrheic not due to anorexia ADD	**Oral contraceptives**	Any available brand of combination oral contraceptive	C[¶]	$13.04
If unable or unwilling to use bisphosphonate USE	**Calcitonin**	calcitonin 100 IU subcutaneously daily	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily	B	$49.00
If immobilized and with acute fracture(s) and not already receiving calcitonin ADD	**Calcitonin**	calcitonin 100 IU subcutaneously for 6-12 weeks	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily for 6-12 weeks	B	$49.00

NOTES:

Other causes of osteoporosis aside from glucocorticoid use should always be considered.

* If < 3 months treat as a glucocorticoid naïve patient (page 26).

† Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods. If combined with etidronate therapy, calcium supplements need not be taken during the 14 days of each cycle when etidronate is given.

‡ The concensus panel strongly recommends this high risk patient population be treated aggressively despite the absence of strong supportive evidence of treatment efficacy in terms of fracture prevention.

§ Bisphosphonate therapy is absolutely contraindicated in pregnancy due its potential teratogenic effects. Contraception should be strongly encouraged in sexually active women.

|| To ease administration of this cyclical regimen, the manufacturer packages etidronate and calcium sequentially in a blister pack format called Didrocal®. Administer 1 Didrocal tablet daily.

References supporting these recommendations: 49,52,54,112

Men without osteoporosis or risk factors

Description: Age ≥ 19 years
AND No previous osteoporotic fracture
AND No other risk factors:

- normal or unknown bone mineral density
- not currently smoking
- no history of hip, wrist or vertebral fractures in a first-degree relative
- no hypogonadism*
- body weight ≥ 57.8 kg or BMI ≥ 21.2 kg/m^2
- not advanced in age (≥ 75 years)
- not institutionalized
- not predisposed to falls

Primary Preventative Therapy:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOMMENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement†	calcium 1000 mg daily	C‡	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	C‡	$2.02

NOTES:

BMI = body mass index (Refer to page 39 for a nomogram to calculate BMI)

* There is no requirement to assess gonadal state with testosterone concentrations if it is unknown.

† Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods.

‡ Recommendations become grade B in patients > 65 years

References supporting these recommendations: 26,115

Men without osteoporosis or risk factors

Description: Age ≥ 19 years
AND No previous osteoporotic fracture
AND No other risk factors:

- normal or unknown bone mineral density
- not currently smoking
- no history of hip, wrist or vertebral fractures in a first-degree relative
- no hypogonadism*
- body weight ≥ 57.8 kg or BMI ≥ 21.2 kg/m^2
- not advanced in age (≥ 75 years)
- not institutionalized
- not predisposed to falls

Primary Preventative Therapy:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement†	calcium 1000 mg daily	C‡	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	C‡	$2.02

NOTES:

BMI = body mass index (Refer to page 39 for a nomogram to calculate BMI)

* There is no requirement to assess gonadal state with testosterone concentrations if it is unknown.

† Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods.

‡ Recommendations become grade B in patients > 65 years

References supporting these recommendations: 26,115

Men without osteoporosis but with risk factors

Description: No previous osteoporotic fracture(s)
AND One or more of the following risk factors:

- T-score between -2.5 SD and -1 SD
- current cigarette smoking
- history of hip, wrist or vertebral fractures in a first-degree relative
- hypogonadism
- small frame (body weight <57.8 kg or BMI <21.2 kg/m)
- advanced in age (≥ 75 years)
- institutionalized
- predisposition to falls

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOMMENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02

Special Circumstances:

If hypogonadal[†] ADD	**Testosterone**	testosterone cypionate or enanthate 200-400 mg intramuscularly every 2-4 weeks	B	$22.85 to $92.84
		OR		
		testosterone undecanoate 40-80 mg PO 3 times daily with food	B	$85.78 to $171.55
If T score between –1 SD and –2.5 SD or unknown ADD	**Bisphosphonate**[‡]	alendronate 10 mg daily	C	$52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)[‡]	C	$12.23
		OR		
		risedronate 5 mg daily	C	$50.49

Men without osteoporosis but with risk factors

Description: No previous osteoporotic fracture(s)
AND One or more of the following risk factors:

- T-score between -2.5 SD and -1 SD
- current cigarette smoking
- history of hip, wrist or vertebral fractures in a first-degree relative
- hypogonadism
- small frame (body weight <57.8 kg or BMI <21.2 kg/m^2)
- advanced in age (≥ 75 years)
- institutionalized
- predisposition to falls

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOMMENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02

Special Circumstances:

If hypogonadal[†] ADD	**Testosterone**	testosterone cypionate or enanthate 200-400 mg intramuscularly every 2-4 weeks	B	$22.85 to $92.84
		OR		
		testosterone undecanoate 40-80 mg PO 3 times daily with food	B	$85.78 to $171.55
If T score between –1 SD and –2.5 SD or unknown ADD	**Bisphosphonate**[‡]	alendronate 10 mg daily	C	$52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)[§]	C	$12.23
		OR		
		risedronate 5 mg daily	C	$50.49

NOTES:

BMI = body mass index (Refer to page 39 for a nomogram to calculate BMI)

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods. If combined with etidronate therapy, calcium supplements need not be taken during the 14 days of each cycle when etidronate is given.

† Routine screening of testosterone is not recommended in the absence of clinical findings suggestive of hypogonadism. Bioavailable testosterone is the preferred test since free testosterone is less sensitive.

‡ The risks and benefits of longterm bisphosphonate therapy in this patient population are unknown.

§ To ease administration of this cyclical regimen, the manufacturer packages etidronate and calcium sequentially in a blister pack format called Didrocal®. Administer 1 Didrocal tablet daily.

References supporting these recommendations: 26,51,115-117

Glucocorticoid-treated men without osteoporosis

Description: No previous osteoporotic fractures
AND Starting/receiving long term glucocorticoid therapy (≥3 months with ≥7.5 mg/day of prednisone or equivalent)
AND BMD normal (T-score > -2.5 S.D.) or unknown

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Bisphosphonate**	alendronate 5-10 mg daily† OR	B	$41.48 to $52.65
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)‡	B	$12.23
		risedronate 5 mg daily	B	$50.49

Special Circumstances:

If hypogonadal ADD	**Testosterone**	testosterone cypionate or enanthate 200-400 mg intramuscularly every 2-4 weeks OR	B	$22.85 to $92.84
		testosterone undecanoate 40-80 mg PO 3 times daily with food	B	$85.78 to $171.55

NOTES:

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods. If combined with etidronate therapy, calcium supplements need not be taken during the 14 days of each cycle when etidronate is given.

† Patients should be started at alendronate 10 mg daily for the first year.

‡ To ease administration of this cyclical regimen, the manufacturer packages etidronate and calcium sequentially in a blister pack format called Didrocal®. Administer 1 Didrocal tablet daily.

References supporting these recommendations: 26,49,52,54,61,115-119

Men with osteoporosis

Description: Previous osteoporotic fracture **or** T-score < -2.5 SD
AND With or without long term glucocorticoid therapy (≥ 3 months with ≥ 7.5 mg/day of prednisone or equivalent)

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOMMENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Bisphosphonate**	alendronate 10 mg daily	B	$52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)‡	C	$12.23
		OR		
		risedronate 5 mg daily	C	$50.49

Special Circumstances:

If hypogonadal ADD	**Testosterone**	testosterone cypionate or enanthate 200-400 mg intramuscularly every 2-4 weeks	C	$22.85 to $92.84
		OR		
		testosterone undecanoate 40-80 mg PO 3 times daily with food	C	$85.78 to $171.55
If immobilized and with acute fracture(s) ADD	**Calcitonin**	calcitonin 100 IU subcutaneously for 6-12 weeks	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily for 6-12 weeks	B	$49.00

Glucocorticoid-treated men without osteoporosis

Description: No previous osteoporotic fractures
AND Starting/receiving long term glucocorticoid therapy (≥3 months with ≥7.5 mg/day of prednisone or equivalent)
AND BMD normal (T-score > -2.5 S.D.) or unknown

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Bisphosphonate**	alendronate 5-10 mg daily† OR	B	$41.48 to $52.65
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)‡	B	$12.23
		risedronate 5 mg daily	B	$50.49

Special Circumstances:

If hypogonadal ADD	**Testosterone**	testosterone cypionate or enanthate 200-400 mg intramuscularly every 2-4 weeks OR	B	$22.85 to $92.84
		testosterone undecanoate 40-80 mg PO 3 times daily with food	B	$85.78 to $171.55

NOTES:

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods. If combined with etidronate therapy, calcium supplements need not be taken during the 14 days of each cycle when etidronate is given.

† Patients should be started at alendronate 10 mg daily for the first year.

‡ To ease administration of this cyclical regimen, the manufacturer packages etidronate and calcium sequentially in a blister pack format called Didrocal®. Administer 1 Didrocal tablet daily.

References supporting these recommendations: 26,49,52,54,61,115-119

Men with osteoporosis

Description: Previous osteoporotic fracture **or** T-score < -2.5 SD
AND With or without long term glucocorticoid therapy (≥ 3 months with ≥ 7.5 mg/day of prednisone or equivalent)

Recommended Therapies:

	RECOMMENDED AGENTS	SUGGESTED REGIMEN	GRADE OF RECOM-MENDATION	ESTIMATED AVERAGE MONTHLY COST
	Calcium supplement*	calcium 1000 mg daily	B	$2.19
AND	**Vitamin D supplement**	vitamin D 800 IU daily	B	$2.02
AND	**Bisphosphonate**	alendronate 10 mg daily	B	$52.65
		OR		
		etidronate 400 mg daily for 14 days followed by calcium 500 mg (elemental) daily for next 76 days (repeat cycle)[1]	C	$12.23
		OR		
		risedronate 5 mg daily	C	$50.49

Special Circumstances:

If hypogonadal ADD	**Testosterone**	testosterone cypionate or enanthate 200-400 mg intramuscularly every 2-4 weeks	C	$22.85 to $92.84
		OR		
		testosterone undecanoate 40-80 mg PO 3 times daily with food	C	$85.78 to $171.55
If immobilized and with acute fracture(s) ADD	**Calcitonin**	calcitonin 100 IU subcutaneously for 6-12 weeks	B	$261.64
		OR		
		calcitonin 200 IU intranasally daily for 6-12 weeks	B	$49.00

NOTES:

Secondary causes should be considered, particularly in men < 75 years old (e.g. alcoholism, hypogonadism).

* Assuming the average daily dietary intake of calcium is 500 mg. Refer to page 40 for calcium content of select foods. If combined with etidronate therapy, calcium supplements need not be taken during the 14 days of each cycle when etidronate is given.

† To ease administration of this cyclical regimen, the manufacturer packages etidronate and calcium sequentially in a blister pack format called Didrocal®. Administer 1 Didrocal tablet daily.

References supporting these recommendations: 9,26,49,52,54,55,115-123

Section III

Treatment Modalities

Ontario Program for Optimal Therapeutics

M121

IMPORTANT NOTE CONCERNING THE FOLLOWING PAGES

THE PAGES WHICH FOLLOW HAVE BEEN FILMED TWICE IN ORDER TO OBTAIN THE BEST REPRODUCTIVE QUALITY

USERS SHOULD CONSULT ALL THE PAGES REPRODUCED ON THE FICHE IN ORDER TO OBTAIN A COMPLETE READING OF THE TEXT.

REMARQUE IMPORTANTE CONCERNANT LES PAGES QUI SUIVENT

LES PAGES SUIVANTES ONT ÉTÉ REPRODUITES EN DOUBLE AFIN D'AMÉLIORER LA QUALITÉ DE REPRODUCTION

LES UTILISATEURS DOIVENT CONSULTER TOUTES LES PAGES REPRODUITES SUR LA FICHE AFIN D'OBTENIR LA LECTURE DU TEXTE INTÉGRAL

micromedia
a division of IHS Canada

20 Victoria Street
Toronto, Ontario M5C 2N8
Tel.: (416) 362-5211
Toll Free: 1-800-387-2689
Fax: (416) 362-6161
Email: info@micromedia.on.ca

Treatment Modalities

Table 2 – Drug Treatments with Available Doses and Corresponding Costs

DRUG	DOSAGES	ESTIMATED AVERAGE MONTHLY COSTS
Calcium		
calcium (calcium carbonate, calcium gluconate, calcium citrate, calcium glucoheptonate, calcium lactate, etc)	500 mg (elemental) daily	$1.10
	1 g (elemental) daily	$2.19
	1.5 g (elemental) daily	$3.29
Vitamin D		
vitamin D	800 iu daily*	$2.02
calcitriol	0.25 mcg daily	$26.74
	0.5 mcg daily	$42.52
Estrogen		
congugated estrogens (Premarin®, C.E.S.®)	0.625 mg daily	$2.35
ethinyl estradiol (Estinyl®)	0.02 mg daily	$2.54
	0.05 mg daily	$4.19
estrone sulphate (Ogen®)	0.625 mg daily	$4.26
micronized estradiol-17β (Estrace®)	0.5 mg daily	$10.04
transdermal estradiol-17β gel (Estrogel®)	Apply daily	$17.95
transdermal estradiol (Estraderm®, Vivelle®, Climara®, Oesclim®)	50 mcg (per 24 hours)	$21.13
	100 mcg (per 24 hours)	$23.83
	Apply either patch twice weekly	
Progestogens		
medroxyprogesterone acetate (Provera®)	2.5 mg daily	$2.49
	5 mg daily	$4.93
norethindrone (Micronor®)	0.35 mg daily	$12.21
micronized progesterone (Prometrium®)	100 mg daily	$11.95
	200 mg daily	$23.90
	300 mg daily	$35.85
Oral Contraceptives	daily	$13.04
Selective Estrogen Receptor Modulators (SERM's)		
raloxifene (Evista®)	60 mg daily	$43.68
Bisphosphonates		
etidronate/calcium carbonate (Didrocal®)	400 mg / 500 mg daily	$12.23
alendronate (Fosamax®)	5 mg daily	$41.48
	10 mg daily	$52.65
risedronate (Actonel®)	5 mg daily	$50.49
Calcitonin		
calcitonin salmon (Calcimar®, Caltine®)	100 iu inject SQ daily	$261.64
synthetic calcitonin; salmon (Miacalcin NS®)	200 iu intranasally daily	$49.00
Testosterone		
testosterone cypionate or enanthate (Depo-Testosterone®, Delatestryl®)	200 mg I.M. every 4 weeks	$22.85
	400 mg I.M. every 2 weeks	$92.84
testosterone undecanoate (Andriol®)	40 mg PO three times daily	$85.78
	80 mg PO three times daily	$171.55

NOTE:

* often available as a 400 iu capsules, therefore 2 capsules may be required.

Treatment Modalities

Table 2 – Drug Treatments with Available Doses and Corresponding Costs

DRUG	DOSAGES	ESTIMATED AVERAGE MONTHLY COSTS
Calcium		
calcium (calcium carbonate, calcium gluconate, calcium citrate, calcium glucoheptonate, calcium lactate, etc)	500 mg (elemental) daily	$1.10
	1 g (elemental) daily	$2.19
	1.5 g (elemental) daily	$3.29
Vitamin D		
vitamin D	800 iu daily*	$2.02
calcitriol	0.25 mcg daily	$26.74
	0.5 mcg daily	$42.52
Estrogen		
congugated estrogens (Premarin®, C.E.S.®)	0.625 mg daily	$2.35
ethinyl estradiol (Estinyl®)	0.02 mg daily	$2.54
	0.05 mg daily	$4.19
estrone sulphate (Ogen®)	0.625 mg daily	$4.26
micronized estradiol-17β (Estrace®)	0.5 mg daily	$10.04
transdermal estradiol-17β gel (Estrogel®)	Apply daily	$17.95
transdermal estradiol (Estraderm®, Vivelle®, Climara®, Oesclim®)	50 mcg (per 24 hours)	$21.13
	100 mcg (per 24 hours)	$23.83
	Apply either patch twice weekly	
Progestogens		
medroxyprogesterone acetate (Provera®)	2.5 mg daily	$2.49
	5 mg daily	$4.93
norethindrone (Micronor®)	0.35 mg daily	$12.21
micronized progesterone (Prometrium®)	100 mg daily	$11.95
	200 mg daily	$23.90
	300 mg daily	$35.85
Oral Contraceptives	daily	$13.04
Selective Estrogen Receptor Modulators (SERM's)		
raloxifene (Evista®)	60 mg daily	$43.68
Bisphosphonates		
etidronate/calcium carbonate (Didrocal®)	400 mg / 500 mg daily	$12.23
alendronate (Fosamax®)	5 mg daily	$41.48
	10 mg daily	$52.65
risedronate (Actonel®)	5 mg daily	$50.49
Calcitonin		
calcitonin salmon (Calcimar®, Caltine®)	100 iu inject SQ daily	$261.64
synthetic calcitonin; salmon (Miacalcin NS®)	200 iu intranasally daily	$49.00
Testosterone		
testosterone cypionate or enanthate (Depo-Testosterone®, Delatestryl®)	200 mg I.M. every 4 weeks	$22.85
	400 mg I.M. every 2 weeks	$92.84
testosterone undecanoate (Andriol®)	40 mg PO three times daily	$85.78
	80 mg PO three times daily	$171.55

NOTE:

* often available as a 400 iu capsules, therefore 2 capsules may be required.

Hormone Replacement Therapy Selection and Dosing

It is desirable with estrogen supplementation to use the lowest effective dose in order to minimize potential adverse effects. Daily doses of 0.625 mg of conjugated estrogens (or equivalent) has traditionally been recommended as the lowest effective dose for most women[124]. There are data suggesting that a 0.3 mg dose of conjugated estrogens (or equivalent) combined with calcium and vitamin D is as effective as higher doses[125]. Estrogen can be administered as a continuous combined regimen where low dose estrogen and progestogen are administered continuously. Alternatively, a cyclical regimen may be used, where estrogen is administered for 21 to 25 days while progestogen is administered for the last 12-14 days of the estrogen course. A 5 to 7 day rest period follows. Continuous combined regimens may be most acceptable to some women (e.g. older women) where amenorrhea usually occurs within 12 months of use[16].

Alternative estrogen products with approximate dosage equivalents and respective costs[24]

Estrogen Product	Maintenance dose for cyclical and continuous regimens	Cost
conjugated estrogens	0.625 mg daily	$2.35
ethinyl estradiol	0.02-0.05 mg daily	$2.54 to $4.19
estrone sulfate	0.625 mg daily	$4.26
micronized estradiol-17β	0.5 mg daily	$10.04
estradiol-17β gel	Metered dose from pump daily	$17.95
estradiol patch	50-100 ug apply patch twice weekly	$21.13 to $23.83

Alternative progestin products with approximate dosage equivalents and respective costs[24]

Progestin Product	Maintenance dose for cyclical regimens (12-14 days per month)	Maintenance dose for continuous regimen	Cost of a continuous regimen
medroxyprogesterone acetate	2.5 -10 mg daily	1.25-5 mg daily	$1.24 to $4.93
norethindrone	0.35-0.70 mg daily	0.175-0.35 mg daily	$6.10 to $12.21
micronized progesterone	200-300 mg daily	100-200 mg daily	$11.95 to $23.90

Body Mass Index (kg/m^2) Nomogram

Height (Meters)	Weight (Kg) 45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125	130
1.50	20.0	22.2	24.4	26.7	28.9	31.1	33.3	35.6	37.8	40.0	42.2	44.4	46.7	48.9	51.1	53.3	55.6	57.8
1.55	18.7	20.8	22.9	25.0	27.1	29.1	31.2	33.3	35.4	37.5	39.5	41.6	43.7	45.8	47.9	49.9	52.0	54.1
1.60	17.6	19.5	21.5	23.4	25.4	27.3	29.3	31.3	33.2	35.2	37.1	39.1	41.0	43.0	44.9	46.9	48.8	50.8
1.65	16.5	18.4	20.2	22.0	23.9	25.7	27.5	29.4	31.2	33.1	34.9	36.7	38.6	40.4	42.2	44.1	45.9	47.8
1.70	15.6	17.3	19.0	20.8	22.5	24.2	26.0	27.7	29.4	31.1	32.9	34.6	36.3	38.1	39.8	41.5	43.3	45.0
1.75	14.7	16.3	18.0	19.6	21.2	22.9	24.5	26.1	27.8	29.4	31.0	32.7	34.3	35.9	37.6	39.2	40.8	42.4
1.80	13.9	15.4	17.0	18.5	20.1	21.6	23.1	24.7	26.2	27.8	29.3	30.9	32.4	34.0	35.5	37.0	38.6	40.1
1.85	13.1	14.6	16.1	17.5	19.0	20.5	21.9	23.4	24.8	26.3	27.8	29.2	30.7	32.1	33.6	35.1	36.5	38.0
1.90	12.5	13.9	15.2	16.6	18.0	19.4	20.8	22.2	23.5	24.9	26.3	27.7	29.1	30.5	31.9	33.2	34.6	36.0
1.95	11.8	13.1	14.5	15.8	17.1	18.4	19.7	21.0	22.4	23.7	25.0	26.3	27.6	28.9	30.2	31.6	32.9	34.2
2.00	11.3	12.5	13.8	15.0	16.3	17.5	18.8	20.0	21.3	22.5	23.8	25.0	26.3	27.5	28.8	30.0	31.3	32.5
2.05	10.7	11.9	13.1	14.3	15.5	16.7	17.8	19.0	20.2	21.4	22.6	23.8	25.0	26.2	27.4	28.6	29.7	30.9
2.10	10.2	11.3	12.5	13.6	14.7	15.9	17.0	18.1	19.3	20.4	21.5	22.7	23.8	24.9	26.1	27.2	28.3	29.5
2.15	9.7	10.8	11.9	13.0	14.1	15.1	16.2	17.3	18.4	19.5	20.6	21.6	22.7	23.8	24.9	26.0	27.0	28.1
2.20	9.3	10.3	11.4	12.4	13.4	14.5	15.5	16.5	17.6	18.6	19.6	20.7	21.7	22.7	23.8	24.8	25.8	26.9
2.25	8.9	9.9	10.9	11.9	12.8	13.8	14.8	15.8	16.8	17.8	18.8	19.8	20.7	21.7	22.7	23.7	24.7	25.7
2.30	8.5	9.5	10.4	11.3	12.3	13.2	14.2	15.1	16.1	17.0	18.0	18.9	19.8	20.8	21.7	22.7	23.6	24.6

NOTE: Ideal body mass index: 20-24.9 (shaded area)

Hormone Replacement Therapy Selection and Dosing

It is desirable with estrogen supplementation to use the lowest effective dose in order to minimize potential adverse effects. Daily doses of 0.625 mg of conjugated estrogens (or equivalent) has traditionally been recommended as the lowest effective dose for most women[124]. There are data suggesting that a 0.3 mg dose of conjugated estrogens (or equivalent) combined with calcium and vitamin D is as effective as higher doses[125]. Estrogen can be administered as a continuous combined regimen where low dose estrogen and progestogen are administered continuously. Alternatively, a cyclical regimen may be used, where estrogen is administered for 21 to 25 days while progestogen is administered for the last 12-14 days of the estrogen course. A 5 to 7 day rest period follows. Continuous combined regimens may be most acceptable to some women (e.g. older women) where amenorrhea usually occurs within 12 months of use[16].

Alternative estrogen products with approximate dosage equivalents and respective costs[24]

Estrogen Product	Maintenance dose for cyclical and continuous regimens	Cost
conjugated estrogens	0.625 mg daily	$2.35
ethinyl estradiol	0.02-0.05 mg daily	$2.54 to $4.19
estrone sulfate	0.625 mg daily	$4.26
micronized estradiol-17β	0.5 mg daily	$10.04
estradiol-17β gel	Metered dose from pump daily	$17.95
estradiol patch	50-100 ug apply patch twice weekly	$21.13 to $23.83

Alternative progestin products with approximate dosage equivalents and respective costs[24]

Progestin Product	Maintenance dose for cyclical regimens (12-14 days per month)	Maintenance dose for continuous regimen	Cost of a continuous regimen
medroxyprogesterone acetate	2.5 -10 mg daily	1.25-5 mg daily	$1.24 to $4.93
norethindrone	0.35-0.70 mg daily	0.175-0.35 mg daily	$6.10 to $12.21
micronized progesterone	200-300 mg daily	100-200 mg daily	$11.95 to $23.90

Body Mass Index (kg/m^2) Nomogram

Height (Meters) \ Weight (Kg)	45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125	130
1.50	20.0	22.2	24.4	26.7	28.9	31.1	33.3	35.6	37.8	40.0	42.2	44.4	46.7	48.9	51.1	53.3	55.6	57.8
1.55	18.7	20.8	22.9	25.0	27.1	29.1	31.2	33.3	35.4	37.5	39.5	41.6	43.7	45.8	47.9	49.9	52.0	54.1
1.60	17.6	19.5	21.5	23.4	25.4	27.3	29.3	31.3	33.2	35.2	37.1	39.1	41.0	43.0	44.9	46.9	48.8	50.8
1.65	16.5	18.4	20.2	22.0	23.9	25.7	27.5	29.4	31.2	33.1	34.9	36.7	38.6	40.4	42.2	44.1	45.9	47.8
1.70	15.6	17.3	19.0	20.8	22.5	24.2	26.0	27.7	29.4	31.1	32.9	34.6	36.3	38.1	39.8	41.5	43.3	45.0
1.75	14.7	16.3	18.0	19.6	21.2	22.9	24.5	26.1	27.8	29.4	31.0	32.7	34.3	35.9	37.6	39.2	40.8	42.4
1.80	13.9	15.4	17.0	18.5	20.1	21.6	23.1	24.7	26.2	27.8	29.3	30.9	32.4	34.0	35.5	37.0	38.6	40.1
1.85	13.1	14.6	16.1	17.5	19.0	20.5	21.9	23.4	24.8	26.3	27.8	29.2	30.7	32.1	33.6	35.1	36.5	38.0
1.90	12.5	13.9	15.2	16.6	18.0	19.4	20.8	22.2	23.5	24.9	26.3	27.7	29.1	30.5	31.9	33.2	34.6	36.0
1.95	11.8	13.1	14.5	15.8	17.1	18.4	19.7	21.0	22.4	23.7	25.0	26.3	27.6	28.9	30.2	31.6	32.9	34.2
2.00	11.3	12.5	13.8	15.0	16.3	17.5	18.8	20.0	21.3	22.5	23.8	25.0	26.3	27.5	28.8	30.0	31.3	32.5
2.05	10.7	11.9	13.1	14.3	15.5	16.7	17.8	19.0	20.2	21.4	22.6	23.8	25.0	26.2	27.4	28.6	29.7	30.9
2.10	10.2	11.3	12.5	13.6	14.7	15.9	17.0	18.1	19.3	20.4	21.5	22.7	23.8	24.9	26.1	27.2	28.3	29.5
2.15	9.7	10.8	11.9	13.0	14.1	15.1	16.2	17.3	18.4	19.5	20.6	21.6	22.7	23.8	24.9	26.0	27.0	28.1
2.20	9.3	10.3	11.4	12.4	13.4	14.5	15.5	16.5	17.6	18.6	19.6	20.7	21.7	22.7	23.8	24.8	25.8	26.9
2.25	8.9	9.9	10.9	11.9	12.8	13.8	14.8	15.8	16.8	17.8	18.8	19.8	20.7	21.7	22.7	23.7	24.7	25.7
2.30	8.5	9.5	10.4	11.3	12.3	13.2	14.2	15.1	16.1	17.0	18.0	18.9	19.8	20.8	21.7	22.7	23.6	24.6

NOTE: Ideal body mass index: 20-24.9 (shaded area)

Table 3 -Approximate Calcium Content of Select Foods

(ideal daily intake ≥ 1500 mg)

Food	Portion	Calcium Content (mg)[126]
DAIRY PRODUCTS		
Milk (skim, 1%, 2%, homogenized)	1 cup/250 mL	300
Buttermilk or chocolate milk	1 cup/250 mL	285
Soy beverage	1 cup/250 mL	10
Ice Cream	½ cup/125 mL	80
Light sour cream	1 tbsp/50 mL	30
Sour cream	1 tbsp/50 mL	15
Plain yogurt	¾ cup/175 g	300
Fruit yogurt	¾ cup/175 g	250
Swiss cheese	1 ¾ oz/50 g	480
Light cheddar cheese	1 ¾ oz/50 g	385
Cheddar cheese	1 ¾ oz/50 g	360
Grated Parmesan cheese	1 tbsp/15 mL	85
Cottage cheese	½ cup/125 mL	75
BREAD		
White bread	1 slice	20
Whole wheat bread	1 slice	24
FRUIT		
Figs, dried, chopped	½ cup/250 mL	120
Currants, dried, chopped	½ cup/250 mL	60
Raisins	½ cup/250 mL	40
Apricots, dried, chopped	½ cup/250 mL	30
Dates, dried, chopped	½ cup/250 mL	30
Oranges, whole, fresh	1 medium	50
VEGETABLES		
Bok-choy, shredded, raw	½ cup/125 mL	35
Bok-choy, shredded, cooked	½ cup/125 mL	80
Brocoli, chopped, raw	½ cup/125 mL	20
Brocoli, chopped, cooked	½ cup/125 mL	35
Cabbage, shredded, raw	½ cup/125 mL	15
Cabbage, shredded, cooked	½ cup/125 mL	25
Chick-peas, canned or boiled	½ cup/125 mL	75
Kale, chopped, raw	½ cup/125 mL	45
Kidney beans, canned or boiled	½ cup/125 mL	55
Turnip greens, chopped, raw	½ cup/125 mL	105
MEAT, FISH, POULTRY, ALTERNATIVES		
Tuna, canned, drained	7 ½ oz can/ half 213g	23
Turkey, dark meat, roasted, no skin	3 oz/90 g	27
Turkey, light meat, roasted, no skin	3 oz/90 g	16
Chicken, roasted, no skin	3 oz/90 g	13
Egg	1 large	24
Pork, roasted, lean only	3 oz/90 g	24
Tofu, containing 10% of recommended daily intake of calcium per 90 g	½ cup/250 mL cubed	110

Reference List

Ontario Program for Optimal Therapeutics

Reference List

1. Anonymous. Concensus development conference: Prophylaxis and treatment of osteoporosis. American Journal of Medicine 1991; 90:107-110.
2. Anonymous. Consensus development conference: Diagnosis, prophylaxis, and treatment of osteoporosis. American Journal of Medicine 1993; 94:646-650.
3. Anonymous editor. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. 1994; (no 843 of Technical Reports series)
4. Melton LJ, Chrischilles EA, Cooper C, Lane W, Riggs BL. How many women have osteoporosis? Journal of Bone & Mineral Research 1992; 7:1005-1010.
5. Jaglal S. Badley EM, Williams JI, editors. Osteoporotic fractures: Incidence and impact. 1998; 143-156. Toronto: Institute for Clinical Evaluation Sciences.
6. Goeree R, O'Brien B, Petitti DB, Cuddy L, Ferraz M, Adachi J. An assessment of the burden of illness due to osteoporosis in Canada. J Soc Obstet Gynaecol Can 1996; 18 (July suppl):25-35.
7. Scientific Advisory Board OSoC. Clinical practice guidelines for the diagnosis and management of osteoporosis Canadian Medical Association Journal 996; 155:1113-1129.
8. McPhee SJ, Schroeder SA. Tierney Jr LM, McPhee SJ, Papadakis MA, editors. General approach to the patient; health maintenance and disease prevention; and common symptoms. 1997; 36 ed., 2-2. Appleton & Lange.
9. Eastell R, Boyle IT, Compston J, Cooper C, Fogelman I, Francis RM, et al. Management of male osteoporosis: report of the UK Conscensus Group. Q J Med 1998; 91:71-92.
10. Kaufman JM, Devogelaer JP, Ralston F, Rozenberg S, Body JJ, Westhovens R, et al. Prevention and treatment of postmenopausal osteoporosis. National concensus of the "Belgian Bone Club", November 1996. Clinical Rheumatology 1997; 16:343-345.
11. Hailey D, Sampietro-Colom L, Marshall D. The effectiveness of bone density measurement and associated treatments for prevention of fractures. An international collaborative review. International Journal of Technology Assessment in Health Care 1998; 14:237-254.
12. Cummings SR, Black DM, Nevitt MC. Bone density at various sites for prediction of hip fractures. Lancet 1993; 341:72-75.
13. Ross PD, Davis JW, Epstein RS. Pre-existing fractures and bone mass predict vertebral fractures incidence in women. Annals of Internal Medicine 1991; 114:919-923.
14. Sturtridge WC, Lentle B, Hanley D. The use of bone density measurement in the diagnosis and management of osteoporosis. Canadian Medical Association Journal 1996; 155:924-929.
15. Miller PD, Bonnick S, Rosen CJ. Clinical utility of bone mass measurements in adults: Concensus of an international panel. Seminars in Arthritis and Rheumatism 1996; 25:361-372.
16. Josse RG. Effects of ovarian hormone therapy on skeletal and estraskeletal tissues in women. Canadian Medical Association Journal 1996; 155:929-934.
17. Anonymous. Osteoporosis: Review of the evidence for prevention, diagnosis and treatment and cost-effectiveness analysis. Osteoporosis International 1998; 8:S1-S88
18. Farmer ME, Harris T, Madans JH, Wallace R, Cornoni-Huntley J, White LR. Anthropometric indicators and hip fracture. The NHANES I epidemiologic follow-up study. Journal of the American Geriatrics Society 1989; 37:9-16.
19. Grisso JA, Kelsey JL, Strom BL. Risk factors for falls as a cause of hip fracture in women. New England Journal of Medicine 1991; 324:1326-1331.
20. Joakimsen RM, Fonnebo V, Magnus JH, Tollan A, Sogaard AJ. The tromso study: body height, body mass index and fractures. Osteoporosis International 1998; 8:436-442.
21. Johnell O, Gullberg B, Kanis JA, Allander E, Elffors L, Dequeker J, et al. Risk factors for hip fracture in European women: the MEDOS Study. Mediterranean Osteoporosis Study. Journal of Bone & Mineral Research 1995; 10:1802-1815.
22. Cummings SR, Nevitt MC, Browner WS, Stone K, Fox KM, Ensrud KE, et al. Risk factors for hip fracture in white women. Study of Osteoporotic Fractures Research Group [see comments]. New England Journal of Medicine 1995; 332:767-773.

23. Anonymous. Physician's guide to prevention and treatment of osteoporosis. 1998; 8-8. Washington, DC: National Osteoporosis Foundation.

24. Anonymous. Appendix 1: Recommendations for prescribing ovarian hormone therapy. Counselling guidelines for hormone replacement therapy (HRT). Canadian Medical Association Journal 1996; 155:1130-1133.

25. Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. New England Journal of Medicine 1990; 323:878-883.

26. Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. New England Journal of Medicine 1997; 337:670-676.

27. Riis B, Thomsen K, Christiansen C. Does calcium supplementation prevent postmenopausal bone loss? A double-blind, controlled clinical study. New England Journal of Medicine 1987; 316:173-177.

28. Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. Effect of calcium supplementation on bone loss in postmenopausal women. New England Journal of Medicine 1993; 328:460-464.

29. Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, et al. Vitamin D3 and calcium to prevent hip fractures in the elderly women. New England Journal of Medicine 1992; 327:1637-1642.

30. Recker RR, Hinders S, Davies KM, Heaney RP, Stegman MR, Lappe JM, et al. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. Journal of Bone & Mineral Research 1996; 11:1961-1966.

31. Cumming RG, Nevitt MC. Calcium for prevention of osteoporotic fractures in postmenopausal women. Journal of Bone & Mineral Research 1997; 12:1321-1329.

32. Heikkinen AM, Parviainen M, Niskanen L, Komulainen M, Tuppurainen MT, Kroger H, et al. Biochemical bone markers and bone mineral density during postmenopausal hormone replacement therapy with and without vitamin D3: a prospective, controlled, randomized study. Journal of Clinical Endocrinology & Metabolism 1997; 82:2476-2482.

33. Murray TM, Ste-Marie LG. Fluoride therapy for osteoporosis. Canadian Medical Association Journal 1996; 155:949-954.

34. O'Neill S, Eisman J, Glasziou P, Kent GN. The prevention and management of osteoporosis. Consensus statement. Australian National Consensus Conference 1996. Medical Journal of Australia 1997; 167:S2-S15

35. Weiss NS, Ure CL, Ballard J, Williams AR, Daling JR. Decreased risk of fractures of the hip and lowere forearm with postmenopausal use of estrogen. New England Journal of Medicine 1980; 303:1195-1198.

36. Kiel DP, Felson DT, Anderson JJ, Wilson PWF, Moskowitz MA. Hip fracture and the use of estrogen in postmenopausal women. New England Journal of Medicine 1987; 317:1169-1174.

37. Hosking D, Chilvers CE, Christiansen C, Ravn P, Wasnich R, Ross P, et al. Prevention of bone loss with alendronate in postmenopausal women under 60 years of age. Early Postmenopausal Intervention Cohort Study Group. New England Journal of Medicine 1998; 338:485-492.

38. Lufkin EG, Wahner HW, O'Fallon WM, Hodgson SF. Treatment of postmenopausal osteoporosis with transdermal estrogen. Annals of Internal Medicine 1992; 117:1-9.

39. McClung M, Clemmesen B, Daifotis A, Gilchrist NL, Eisman J, Weinstein, et al. Alendronate prevents postmenopausal bone loss in women without osteoporosis. A double-blind, randomized, controlled trial. Alendronate Osteoporosis Prevention Study Group. Annals of Internal Medicine 1998; 128:253-261.

40. Evans RA, Somers NM, Dunstan CR, Royle H, Kos S. The effect of low-dose cyclical etidronate and calcium on bone mass in early postmenopausal women. Osteoporosis International 1993; 3:71-75.

41. Meunier PJ, Confavreux E, Tupinon I, Hardouin C, Delmas PD, Balena R. Prevention of early postmenopausal bone loss with cyclical etidronate therapy (a double-blind, placebo-controlled study and 1-year follow-up). Journal of Clinical Endocrinology & Metabolism 1997; 82:2784-2791.

42. Herd RJ, Balena R, Blake GM, Ryan PJ, Fogelman I. The prevention of early postmenopausal bone loss by cyclical etidronate therapy: a 2-year, double-blind, placebo-controlled study. American Journal of Medicine 1997; 103:92-99.

43. Pouilles JM, Tremollieres F, Roux C, Sebert JL, Alexandre C, Goldberg D, et al. Effects of cyclical etidronate therapy on bone loss in early postmenopausal women who are not undergoing hormonal replacement therapy. Osteoporosis International 1997; 7:213-218.

44. Pols HAP, Felsenberg D, Hanley DA, et al. Multinational, placebo-controlled, randomized trial of the effects of alendronate on bone density and fracture risk in postmenopausal women with low bone mass: results of the FOSIT study. Osteoporosis International 1999; 9:461-468.

45. Delmas PD, Bjarnason NH, Mitlak BH, Ravoux AC, Shah AS, Huster WJ, et al. Effects of raloxifene on bone mineral density, serum cholesterol concentrations, and uterine endometrium in postmenopausal women. New England Journal of Medicine 1997; 337:1641-1647.

46. Lindsay R, Hart DM, Maclean A, Clark AC, Kraszewski A, Garwood J. Bone response to termination of oestrogen treatment. Lancet 1978; 1:1325-1327.

47. Lindsay R, Cosman F, Lobo RA, Walsh BW, Harris ST, Reagan JE, et al. Addition of alendronate to ongoing hormone replacement therapy in the treatment of osteoporosis: a randomized, controlled clinical trial. Journal of Clinical Endocrinology & Metabolism 1999; 84:3076-3081.

48. Wimalawansa SJ. Combined therapy with estrogen and etidronate has an additive effect on bone mineral density in the hip and vertebrae: four-year randomized study. American Journal of Medicine 1995; 99:36-42.

49. Roux C, Oriente P, Laan R, Hughes RA, Ittner J, Goemaere S, et al. Randomized trial of effect of cyclical etidronate in the prevention of corticosteroid-induced bone loss. Ciblos Study Group. Journal of Clinical Endocrinology & Metabolism 1998; 83:1128-1133.

50. Diamond T, McGuigan L, Barbagallo S, Bryant C. Cyclical etidronate plus ergocalciferol prevents glucocorticoid-induced bone loss in postmenopausal women. American Journal of Medicine 1995; 98:459-463.

51. Harris ST, Watts NB, Genant HK, McKeever CD. Effects of risedronate treatment on vertebral and nonvertebral fractures in women with postmenopausal osteoporosis. A randomized controlled trial. JAMA 1999; 282:1344-1352.

52. Adachi JD, Bensen WG, Brown J, Hanley D, Hodsman A, Josse R, et al. Intermittent etidronate therapy to prevent corticosteroid-induced osteoporosis [see comments]. New England Journal of Medicine 1997; 337:382-387.

53. Adachi J, Cranney A, Goldsmith CH, Bensen WG, Bianchi F, Cividino A, et al. Intermittent cyclic therapy with etidronate in the prevention of corticosteroid induced bone loss. Journal of Rheumatology 1994; 21:1922-1926.

54. Saag KG, Emkey R, Schnitzer TJ, Brown JP, Hawkins F, Goemaere S, et al. Alendronate for the prevention and treatment of glucocorticoid-induced osteoporosis. Glucocorticoid-induced osteoporosis intervention study group. New England Journal of Medicine 1998; 339:292-299.

55. Struys A, Snelder AA, Mulder H. Cyclical etidronate reverses bone loss of the spine and proximal femur in patients with established corticosteroid-induced osteoporosis. American Journal of Medicine 1995; 99:235-242.

56. Mulder H, Struys A. Intermittent cyclical etidronate in the prevention of corticosteroid-induced bone loss. British Journal of Rheumatology 1994; 33:348-350.

57. Wolfhagen FH, van Buuren HR, den Ouden JW, Hop WC, van Leeuwen JP, Schalm SW, et al. Cyclical etidronate in the prevention of bone loss in corticosteroid-treated primary biliary cirrhosis. A prospective, controlled pilot study. Journal of Hepatology 1997; 26:325-330.

58. Skingle SJ, Crisp AJ. Increased bone density in patients on steroids with etidronate [letter]. Lancet 1994; 344:543-544.

59. Boutsen Y, Jamart J, Esselinckx W, Stoffel M, Devogelaer JP. Primary prevention of glucocorticoid-induced osteoporosis with intermittent intravenous pamidronate: a randomized trial. Calcified Tissue International 1997; 61:266-271.

60. Gonnelli S, Rottoli P, Cepollaro C, Pondrelli C, Cappiello V, Vagliasindi M, et al. Prevention of corticosteroid-induced osteoporosis with alendronate in sarcoid patients. Calcified Tissue International 1997; 61:382-385.

61. Cohen S, Levy R, Keller M, Sewell KL, Boiling E. Risedronate therapy prevents corticosteroid-induced bone loss: a twelve-month, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. Arthritis & Rheumatism 1999; 42:2309-2318.

62. Nordborg E, Schaufelberger C, Andersson R, Bosaeus I, Bengtsson BA. The ineffectiveness of cyclical oral clodronate on bone mineral density in glucocorticoid-treated patients with giant-cell arteritis. Journal of Internal Medicine 1997; 242:367-371.

63. Pitt P, Li F, Todd P, Webber D. A double blind placebo controlled study to determine the effects of intermittent cyclical etidronate on bone mineral density in patients on long-term oral corticosteroid treatment. Thorax 1998; 53:351-356.

64. Geusens P, Vanhoof J, Stalmans R, Joly J. Cyclic etidronate increases bone density in the spine and hip in postmenopausal women on chronic corticosteroid treatment. A double-blind controlled study. Bone 1997; 20:9S-9S.

65. Worth H, Stammen D, Keck E. Therapy of steroid-induced bone loss in adult asthmatics with calcium, vitamin D, and a diphosphonate. American Journal of Respiratory & Critical Care Medicine 1994; 150:394-397.

66. Reid IR, King AR, Alexander CJ, Ibbertson HK. Prevention of steroid-induced osteoporosis with (3-amino-1-hydroxypropylidene)-1,1-bisphosphonate (APD). Lancet 1988; 1:143-146.

67. Reid D, Cohen S, Pack S, Chines A. Risedronate reduces the incidence of vertebral fractures in patients on chronic corticosteroid therapy. Arthritis & Rheumatism 1998; 41:S136-S136

68. Reid D, Cohen S, Pack S, Chines A. Risedronate is an effective and well-tolerated therapy in both the treatment and prevention of corticosteroid-induced osteoporosis. Bone 1998; 23:2402-2402.

69. Sambrook P, Birmingham J, Kelly P, Kempler S, Nguyen T, Pocock N, et al. Prevention of corticosteroid osteoporosis. A comparison of calcium, calcitriol, and calcitonin. New England Journal of Medicine 1993; 328:1747-1752.

70. Homik J, Suarez-Almazor ME, Shea B, Cranney A, Wells G, Tugwell P. Osteoporosis: Calcium and vitamin D for the treatment of corticosteroid-induced osteoporosis. (Cochrane Library) 1998; 1-8.

71. Buckley LM, Leib ES, Cartularo KS, Vacek PM, Cooper SM. Calcium and vitamin D3 supplementation prevents bone loss in the spine secondary to low-dose corticosteroids in patients with rheumatoid arthritis. A randomized, double-blind, placebo-controlled trial [see comments]. Annals of Internal Medicine 1996; 125:961-968.

72. Lukert BP, Johnson BE, Robinson RG. Estrogen and progesterone replacement therapy reduces glucocorticoide-induced bone loss. Journal of Bone & Mineral Research 1992; 7:1063-1069.

73. Hall GM, Daniels M, Doyle DV, Spector TD. Effect of hormone replacement therapy on bone mass in rheumatoid arthritis patients treated with and without steroids. Arthritis & Rheumatism 1994; 37:1499-1505.

74. Luengo M, Picado C, Del Rio L, Guanabens N, Montserrat JM, Setoain J. Treatment of steroid-induced osteopenia with calcitonin in corticosteroid-dependent asthma. A one-year follow-up study. American Review of Respiratory Disease 1990; 142:104-107.

75. Healey JH, Paget SA, Williams-Russo P, Szatrowski TP, Schneider R, Spiera H, et al. A randomized controlled trial of salmon calcitonin to prevent bone loss in corticosteroid-treated temporal arteritis and polymyalgia rheumatica. Calcified Tissue International 1996; 58:73-80.

76. Adachi JD, Bensen WG, Bell MJ, Bianchi FA, Cividino AA, Craig GL, et al. Salmon calcitonin nasal spray in the prevention of corticosteroid-induced osteoporosis. British Journal of Rheumatology 1997; 36:255-259.

77. Sambrook P, Birmingham J, Kelly P, Kempler S, Nguyen T, Pocock N, et al. Prevention of corticosteroid bone loss. Osteoporosis International 1993; 3 Suppl 1:141-143.

78. Ringe JD, Welzel D. Salmon calcitonin in the therapy of corticoid-induced osteoporosis. European Journal of Clinical Pharmacology 1987; 33:35-39.

79. Luengo M, Pons F, Martinez dOM, Picado C. Prevention of further bone mass loss by nasal calcitonin in patients on long term glucocorticoid therapy for asthma: a two year follow up study. Thorax 1994; 49:1099-1102.

80. Kotaniemi A, Piirainen H, Paimela L, Leirisalo-Repo M, Uoti-Reilama K, Lahdentausta P, et al. Is continuous intranasal salmon calcitonin effective in treating axial bone loss in patients with active rheumatoid arthritis receiving low dose glucocorticoid therapy? Journal of Rheumatology 1996; 23:1875-1879.

81. Bohning W, Ringe JD, Welzel D, Bode V. [Intranasal salmon calcitonin for the prophylaxis of bone mineral loss in steroid-treated chronic obstructive lung diseases]. [German]. Arzneimittel-Forschung 1990; 40:1000-1003.

82. Emkey R, Reading W, Procaccini R, Gaich G. The effect of calcitonin on bone mass in steroid-induced osteoporosis. Arthritis & Rheumatism 1995; 37:S183-S183

83. Ettinger B, Genant HK, Cann CE. Long-term estrogen replacement therapy prevents bone loss and fractures. Annals of Internal Medicine 1985; 102:319-324.

84. Paganini-Hill A, Ross RK, Gerkins VR, Henderson BK. Menopausal Estrogen Therapy and Hip Fractures. Annals of Internal Medicine 1981; 95:28-31.

85. Bone HG, Downs RWJ, Tucci JR, Harris ST, Weinstein RS, Licata AA, et al. Dose-response relationships for alendronate treatment in osteoporotic elderly women. Alendronate Elderly Osteoporosis Study Centers. Journal of Clinical Endocrinology & Metabolism 1997; 82:265-274.

86. Anonymous. Effects of hormone therapy on bone mineral density: results from the postmenopausal estrogen/progestin interventions (PEPI) trial. The Writing Group for the PEPI. JAMA 1996; 276:1389-1396.

87. Christiansen C, Riis BJ. 17 Beta-estradiol and continuous norethisterone: a unique treatment for established osteoporosis in elderly women. Journal of Clinical Endocrinology & Metabolism 1990; 71:836-841.

88. Wimalawansa SJ. A four-year randomized controlled trial of hormone replacement and bisphosphonate, alone or in combination, in women with postmenopausal osteoporosis. American Journal of Medicine 1998; 104:219-226.

89. Cauley JA, Seeley DG, Browner WS, Ensrud K, Kuller LH, Lipschutz RC, et al. Estrogen replacement therapy and mortality among older women. The study of osteoporotic fractures. Archives of Internal Medicine 1997; 157:2181-2187.

90. Grady D, Rubin SM, Petitti DB, Fox CS, Black D. Hormone therapy to prevent disease and prolong life in postmenopausal women. Annals of Internal Medicine 1992; 117:1038-1041.

91. Hulley S, Grady D, Bush T, Furberg C, Herrington D, Riggs B, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/progestin Replacement Study (HERS) Research Group. JAMA 998; 280:650-652.

92. Colditz GA, Stampfer MJ, Willet WC, Hennekens CH, Rosner B, Speizer FE. Propective study of estrogen replacement therapy and risk of breast cancer in postmenopausal women. JAMA 1990; 264:2648-2653.

93. Dupont WD, Page DL. Menopausal estrogen replacement therapy and breast cancer. Archives of Internal Medicine 1991; 151:67-72.

94. Steinberg KK, Thacker SB, Smith SJ, et al. A meta-analysis of the effect of estrogen replacement therapy on breast cancer. JAMA 1991; 265:1985-1990.

95. Karpf DB, Shapiro DR, Seeman E, Ensrud KE, Johnston CCJ, Adami S, et al. Prevention of nonvertebral fractures by alendronate. A meta-analysis. Alendronate Osteoporosis Treatment Study Groups. JAMA 1997; 277:1159-1164.

96. Black DM, Cummings SR, Karpf DB, Cauley JA, Thompson DE, Nevitt MC, et al. Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures. Fracture Intervention Trial Research Group. Lancet 1996; 348:1535-1541.

97. Liberman UA, Weiss SR, Broll J, Minne HW, Quan H, Bell NH, et al. Effect of oral alendronate on bone mineral density and the incidence of fractures in postmenopausal osteoporosis. The Alendronate Phase III Osteoporosis Treatment Study Group. New England Journal of Medicine 1995; 333:1437-1443.

98. Ettinger B, Black D, Mitlak BH, Knickerbocker RK. Reduction of vertebral fracture risk in postmenopausal women with osteoporosi treated with raloxifene. Results from a 3-year randomized clinical trial. JAMA 1999; 282:637-645.

99. Miller PD, Watts NB, Licata AA, Harris ST, Genant HK, Wasnich RD, et al. Cyclical etidronate in the treatment of postmenopausal osteoporosis: efficacy and safety after seven years of treatment. American Journal of Medicine 1997; 103:468-476.

100. Reginster JY, Denis D, Albert A, Deroisy R, Lecart MP, Fontaine MA, et al. 1-Year controlled randomised trial of prevention of early postmenopausal bone loss by intranasal calcitonin. Lancet 1987; 2:1481-1483.

101. Cardona JM, Pastor E. Calcitonin versus etidronate for the treatment of postmenopausal osteoporosis: a meta-analysis of published clinical trials. Osteoporosis International 1997; 7:165-174.

102. Adami S, Baroni MC, Broggini M, Carratelli L, Caruso I, Gnessi L, et al. Treatment of postmenopausal osteoporosis with continuous daily oral alendronate in comparison with either placebo or intranasal salmon calcitonin. Osteoporosis International 1993; 3 Suppl 3:S21-S27

103. Chesnut CH, Silverman C, Andriano K. Salmon calcitonin nasal spray reduces the rate of new vertebral fractures independently of known major pre-treatment risk factors: accrued 5 year analysis of the Proof study. Journal of Bone & Mineral Research 1998; 8:S290

104. Rico H, Revilla M, Hernandez ER, Villa LF, Alvarez dB. Total and regional bone mineral content and fracture rate in postmenopausal osteoporosis treated with salmon calcitonin: a prospective study. Calcified Tissue International 1995; 56:181-185.

105. Rico H, Hernandez ER, Revilla M, Gomez-Castresana F. Salmon calcitonin reduces vertebral fracture rate in postmenopausal crush fracture syndrome. Bone & Mineral 1992; 16:131-138.

106. Reginster JY, Deroisy R, Lecart MP, Sarlet N, Zegels B, Jupsin I, et al. A double-blind, placebo-controlled, dose-finding trial of intermittent nasal salmon calcitonin for prevention of postmenopausal lumbar spine bone loss. American Journal of Medicine 1995; 98:452-458.

107. Arnala I, Saastamoinen J, Alhava EM. Salmon calcitonin in the prevention of bone loss at perimenopause. Bone 1996; 18:629-632.

108. Overgaard K, Hansen MA, Jensen SB, Christiansen C. Effect of salcatonin given intranasally on bone mass and fracture rates in established osteoporosis: a dose-response study. BMJ 1992; 305:556-561.

109. Overgaard K, Riis BJ, Christiansen C, Hansen MA. Effect of salcatonin given intranasally on early postmenopausal bone loss. BMJ 1989; 299:477-479.

110. Overgaard K, Hansen MA, Nielsen VA, Riis BJ, Christiansen C. Discontinuous calcitonin treatment of established osteoporosis—effects of withdrawal of treatment. American Journal of Medicine 1990; 89:1-6.

111. Anonymous editor. Raloxifene reduces the risk of incident vertebral fractures: 24-month interim analysis. (Abstract). 1998;

112. Hergenroeder AC, O'Brian Smith E, Shypailo RBS, Jones LA, Klish WJ, Ellis K. Bone mineral changes in young women with hypothalamic amenorrhea treated with oral contraceptives, medroxyprogesterone, or placebo over 12 months. American Journal of Obstetrics & Gynecology 1997; 176:1017-1025.

113. Recker RR, Davies KM, Hinders SM, Heaney RP. Bone gain in young adult women. JAMA 1992; 268:2403-2408.

114. Hodsman A, Adachi J, Olszynski W. Prevention and management of osteoporosis: concensus statements from the Scientific Advisory Board of the Osteoporosis Society of Canada. 6. Use of bisphosphonates in the treatment of osteoporosis. Canadian Medical Association Journal 1996; 155:945-948.

115. Orwoll ES, Oviatt SK, McClung MR, Deftos LJ, Sexton G. The rate of bone mineral loss in normal men and the effects of calcium and cholecalciferol supplementation. Annals of Internal Medicine 1990; 112:29-34.

116. Behre HM, Kliesch S, Leifke E, Link TM, Nieschlag E. Long-term effect of testosterone therapy on bone mineral density in hypogonadal men. Journal of Clinical Endocrinology & Metabolism 1997; 82:2386-2390.

117. Anderson FH, Francis RM, Bishop JC, Rawlings DJ. Effect of intermittent cyclical disodium etidronate therapy on bone mineral density in men with vertebral fractures. Age & Ageing 1997; 26:359-365.

118. Reid IR, Wattie DJ, Evans MC, Stapleton JP. Testosterone therapy in glucocorticoid-treated men. Archives of Internal Medicine 1996; 156:1173-1177.

119. Anderson FH, Francis RM, Peaston RT, Wastell HJ. Androgen supplementation in eugonadal men with osteoporosis: effects of six months' treatment on markers of bone formation and resorption. Journal of Bone & Mineral Research 1997; 12:472-478.

120. Anderson FH, Francis RM, Faulkner K. Androgen supplementation in eugonadal men with osteoporosis-effects of 6 months of treatment on bone mineral density and cardiovascular risk factors. Bone 1996; 18:171-177.

121. Morley JE, Kaiser FE, Sih R, Hajjar RR. Testosterone and frailty. Clinics in Geriatric Medicine 1997; 13:685-695.

122. Hajjar RR, Kaiser FE, Morley JE. Outcomes of long-term testosterone replacement in older hypogonadal males: A retrospective analysis. Journal of Clinical Endocrinology & Metabolism 1997; 82:3793-3796.

123. Anonymous. Optimal calcium intake. NIH Concensus Development Panel on Optimal Calcium Intake. JAMA 1994; 272:1942-1948.

124. Lindsay R, Hart DM, Clark DM. The minimum effective dose of estrogen for prevention of postmenopausal bone loss. Obstetrics & Gynecology 1984; 63:759-763.

125. Recker RR, Davies KM, Dowd RM, Heaney RP. The effect of low-dose continuous estrogen and progesterone therapy with calcium and vitamin D on bone in elderly women. A randomized, controlled trial. Annals of Internal Medicine 1999; 130:897-904.

126. Main J. Bone Vivante! MacMillan, Toronto 1997: 5-7.